STIC Search Report
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STIC Database Tracking Number: 119425

TO: Edward Ward **Location: 3d14 / 3d11** **Thursday, April 15, 2004** **Art Unit: 1654** **Phone: 272-0586** **Serial Number: 10 / 633616**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

19425

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Edward Wood Examiner #: 69450 Date: April 14, 2004
Art Unit: 1654 Phone Number 571-272-0586 Serial Number: 10/632,346
Mail Box and Bldg/Room Location: 7D14 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Waddington

_____

Earliest Priority Filing Date: _____

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

The cross linkers described below

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Jan	NA Sequence (#)	STN: c
Searcher Phone #: 22504	AA Sequence (#)	Dialog
Searcher Location:	Structure (#): V	Questel/Orbit
Date Searcher Picked Up: 4/15	Bibliographic	Dr Link
Date Completed: 4/15	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time: 10	Patent Family	WWW/Internet
Online Time: 1.25	Other	Other (specify)

PTO-1590 (8-01)

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=> fil reg
FILE 'REGISTRY' ENTERED AT 06:31:49 ON 15 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   13 APR 2004  HIGHEST RN 675103-21-6
DICTIONARY FILE UPDATES:  13 APR 2004  HIGHEST RN 675103-21-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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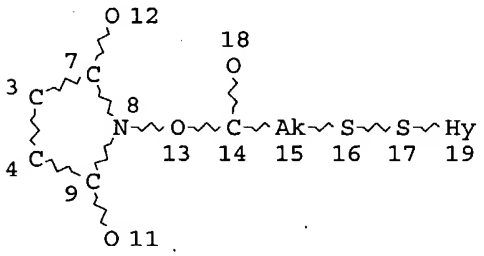


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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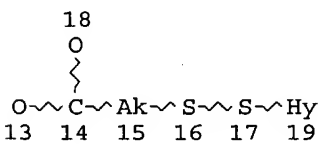


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STEREO ATTRIBUTES: NONE
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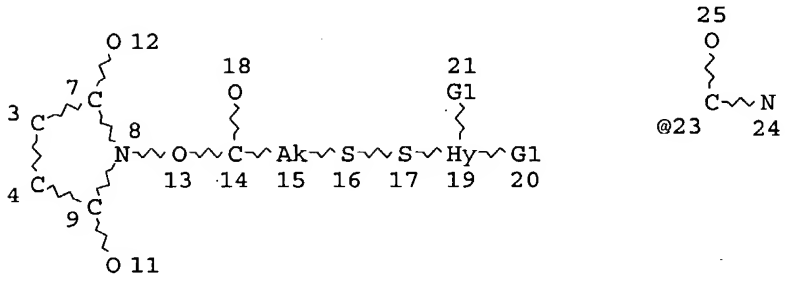


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100.0% PROCESSED     14 ITERATIONS                          0 ANSWERS
SEARCH TIME: 00.00.01


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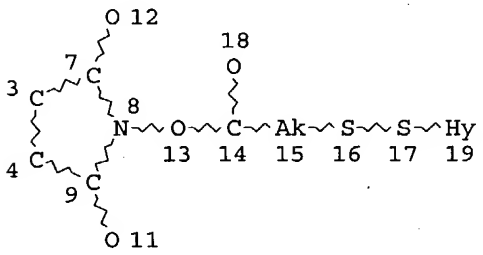


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DEFAULT ECLEVEL IS LIMITED

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STEREO ATTRIBUTES: NONE
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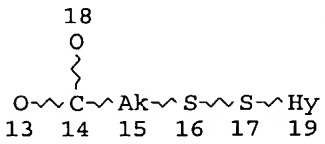

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS   7

STEREO ATTRIBUTES: NONE
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L14           37 SEA FILE=REGISTRY SUB=L13 SSS FUL L7
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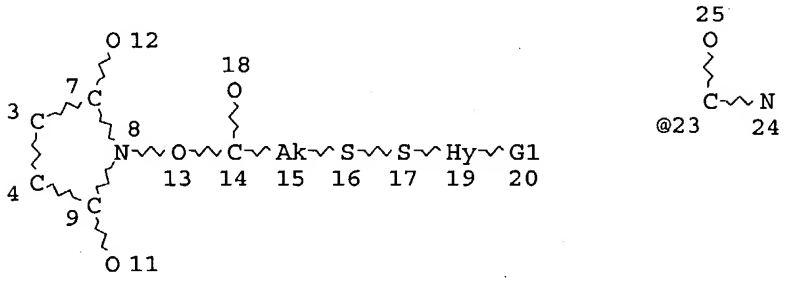


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DEFAULT ECLEVEL IS LIMITED

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100.0% PROCESSED     14 ITERATIONS                          14 ANSWERS
SEARCH TIME: 00.00.01


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               E WIDDISON W/AU
L2            10 S E4,E5
               E IMMUNOGEN/PA,CS
L3           104 S E3-E17
               SEL RN L1

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L4            37 S E1-E37
L5            11 S L4 AND NC5/ES AND NC4/ES
L6            26 S L4 NOT L5
L7               STR
L8             1 S L7
L9               STR L7
L10            1 S L9
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L13         446 S L11 FUL
                SAV L13 WARD633/A
L14          37 S L7 FUL SUB=L13
                SAV L14 WARD633A/A
L15          31 S L14 AND NC5/ES
L16          11 S L5 AND L15
                SAV L15 WARD633B/A

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     FILE 'HCAPLUS' ENTERED AT 06:24:15 ON 15 APR 2004
L18         730 S L15
L19           2 S L2 AND L18
L20           4 S L3 AND L18
L21           4 S L19,L20

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L23           0 S L22 FUL SUB=L15
L24             STR L22
L25          14 S L24 FUL SUB=L15
                SAV L25 WARD633C/A
L26          17 S L15 NOT L25
L27          16 S L26 NOT 68181-17-9
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L29           5 S L25
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L31          12 S L29,L30 AND (?CROSSLINK? OR ?CROSS LINK? OR ?CROSS!LINK?)
L32          26 S L29,L30 AND (?CONJUGAT? OR ?COMPLEX?)
L33          31 S L21,L29-L32
L34          31 S L33 AND (PD<=20020816 OR PRD<=20020816 OR AD<=20020816)

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L35           3 S L25
L36          21 S L28
L37          21 S L35,L36

     FILE 'REGISTRY' ENTERED AT 06:31:49 ON 15 APR 2004

=> fil uspatall
FILE 'USPATFULL' ENTERED AT 06:32:08 ON 15 APR 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

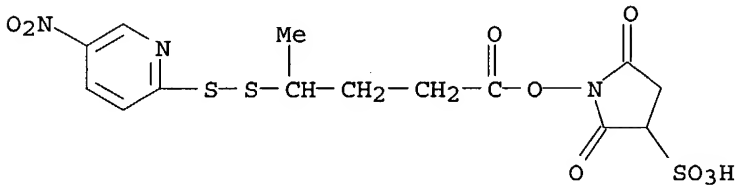
FILE 'USPAT2' ENTERED AT 06:32:08 ON 15 APR 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d l37 bib abs hitstr tot

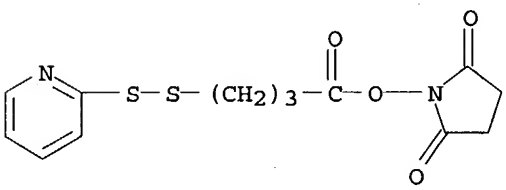
L37  ANSWER 1 OF 21  USPATFULL on STN
AN     2004:51745  USPATFULL
TI     Cross-linkers with high reactivity and solubility and their use in the
       preparation of conjugates for targeted delivery of small molecule drugs
IN     Widdison, Wayne Charles, Somerville, MA, UNITED STATES
PA     Immunogen, Inc. (U.S. corporation)
PI     US 2004039176      A1   20040226
AI     US 2003-633616     A1   20030805 (10)
PRAI   US 2002-403652P     20020816 (60)
DT     Utility
```

FS APPLICATION
LREP SUGHRUE MION, PLLC, 2100 PENNSYLVANIA AVENUE, N.W., WASHINGTON, DC, 20037
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 8 Drawing Page(s)
LN.CNT 1518
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed is a method of making conjugates of cell binding agents and small molecule drugs comprising reacting a cell binding agent with a bifunctional cross-linking moiety to thereby provide the cell binding agent with a reactive disulfide group and then reacting the modified cell binding agent with a small molecule drug comprising a free thiol group. Bifunctional cross-linking moieties are also disclosed.

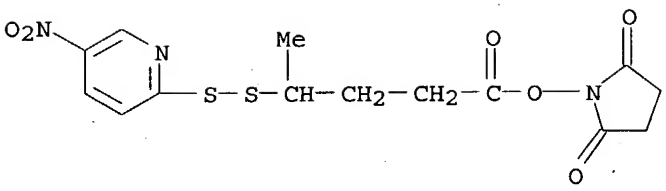
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **663598-66-1DP**, salts
(preparation of succinimidylpyridyldithio carboxylic acid ester crosslinkers and their conjugates with antibodies and small cytotoxic agents for targeted delivery)
RN 663598-66-1 USPATFULL
CN 3-Pyrrolidinesulfonic acid, 1-[[4-[(5-nitro-2-pyridinyl)dithio]-1-oxopentyl]oxy]-2,5-dioxo- (9CI) (CA INDEX NAME)



(prepn. of succinimidylpyridyldithio carboxylic acid ester crosslinkers and their conjugates with antibodies and small cytotoxic agents for targeted delivery)
IT **115088-06-7P 663598-61-6P 663598-85-4P**
663598-89-8DP, salts **663598-98-9P 663599-00-6DP**
, salts **663599-05-1P 663599-07-3DP**, salts
663599-10-8P 663599-11-9DP, salts
(preparation of succinimidylpyridyldithio carboxylic acid ester crosslinkers for conjugating with antibodies and small cytotoxic agents for targeted delivery)
RN 115088-06-7 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-4-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



RN 663598-61-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[[4-[(5-nitro-2-pyridinyl)dithio]-1-oxopentyl]oxy]- (9CI) (CA INDEX NAME)



RN 663598-85-4 USPATFULL
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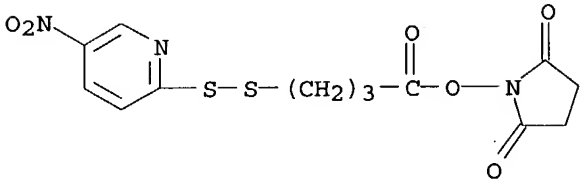

RN 663598-89-8 USPATFULL
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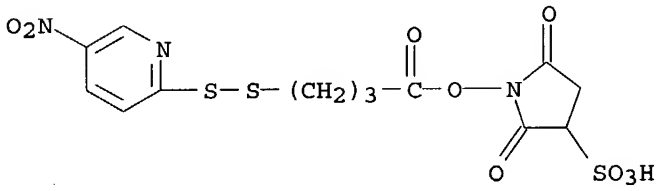

RN 663598-98-9 USPATFULL
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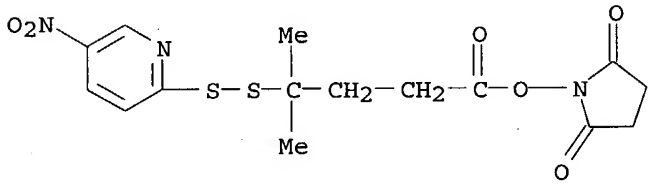
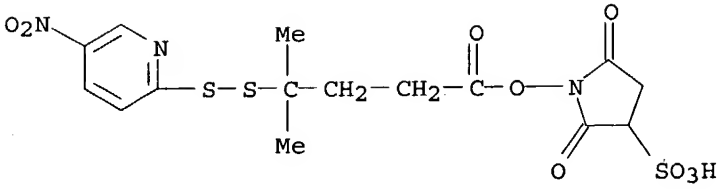
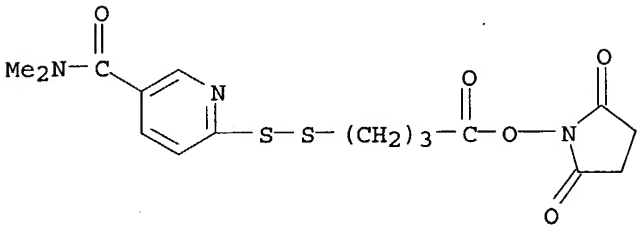


RN 663599-00-6 USPATFULL
CN 3-Pyrrolidinesulfonic acid, 1-[[4-methyl-4-[(5-nitro-2-pyridinyl)dithio]-1-oxopentyl]oxy]-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 663599-05-1 USPATFULL
CN 3-Pyridinecarboxamide, 6-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]dithio]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 663599-07-3 USPATFULL
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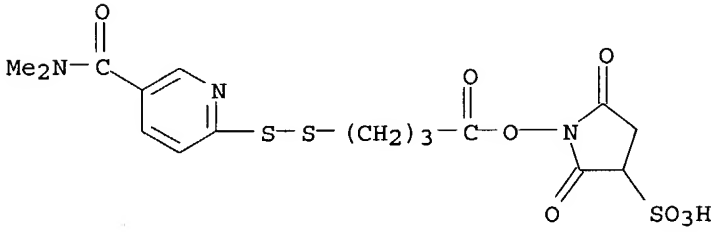
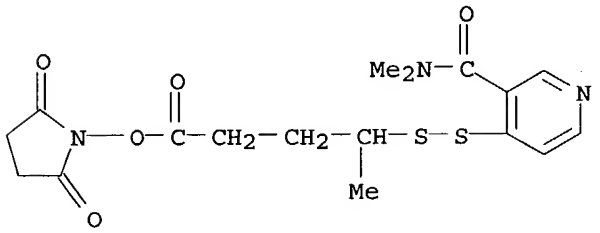


RN 663599-10-8 USPATFULL
CN 3-Pyridinecarboxamide, 4-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-methyl-4-oxobutyl]dithio]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 663599-11-9 USPATFULL
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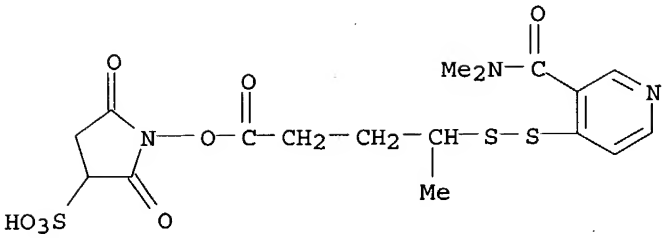
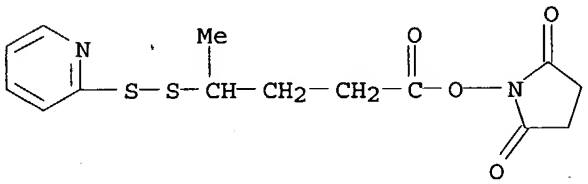
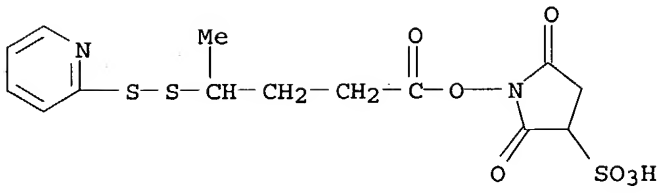


L37 ANSWER 2 OF 21 USPATFULL on STN
AN 2003:79298 USPATFULL
TI Methods for preparation of cytotoxic conjugates of maytansinoids and cell binding agents
IN Chari, Ravi V. J., Newton, MA, UNITED STATES
Widdison, Wayne C., Somerville, MA, UNITED STATES
PA IMMUNOGEN, INC. (U.S. corporation)
PI US 2003055226 A1 20030320
AI US 2002-161651 A1 20020605 (10)
RLI Division of Ser. No. US 2001-867598, filed on 31 May 2001, GRANTED, Pat. No. US 6441163
DT Utility
FS APPLICATION
LREP SUGHRUE, MION, ZINN, MACPEAK &SEAS, PLLC, 2100 Pennsylvania Avenue, N.W., Washington, DC, 20037-3213
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 1010
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses a one-step process for the production of cytotoxic conjugates of maytansinoids and cell binding agents. Maytansinoids having a disulfide linker that bears a reactive moiety are linked to cell binding agents, such as antibodies, without prior modification of the cell binding agent. These conjugates are useful as therapeutic agents which are delivered specifically to target cells and are cytotoxic.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **341498-08-6P 452072-24-1P 452072-27-4P**
(process for preparation of cytotoxic conjugates of maytansinoid derivs. having a disulfide moiety and huN901 antibody)
RN 341498-08-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



RN 452072-24-1 USPATFULL
CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]-, sodium salt (9CI) (CA INDEX NAME)



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RN 452072-27-4 USPATFULL
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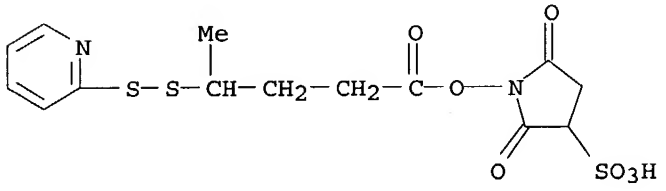
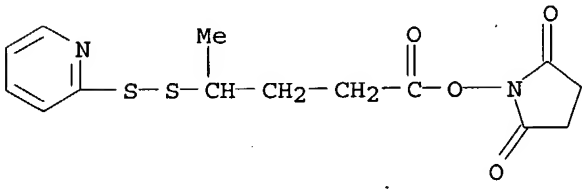


L37 ANSWER 3 OF 21 USPATFULL on STN
AN 2003:4169 USPATFULL
TI Cytotoxic agents comprising taxanes and their therapeutic use
IN Chari, Ravi V.J., Newton, MA, UNITED STATES
Blattler, Walter A., Brookline, MA, UNITED STATES
PA IMMUNOGEN INC. (U.S. corporation)
PI US 2003004210 A1 20030102
US 6706708 B2 20040316
AI US 2002-207814 A1 20020731 (10)
RLI Division of Ser. No. US 2002-59022, filed on 30 Jan 2002, GRANTED, Pat. No. US 6436931 Division of Ser. No. US 2001-933018, filed on 21 Aug 2001, GRANTED, Pat. No. US 6372738 Division of Ser. No. US 2000-717026, filed on 22 Nov 2000, GRANTED, Pat. No. US 6340701
PRAI US 1999-167228P 19991124 (60)
DT Utility
FS APPLICATION
LREP SUGHRUE MION, PLLC, 2100 Pennsylvania Avenue, NW, Washington, DC, 20037-3213
CLMN Number of Claims: 44
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1285
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A cytotoxic agent comprising one or more taxanes linked to a cell binding agent. A therapeutic composition for killing selected cell populations comprising: (A) a cytotoxic amount of one or more taxanes covalently bonded to a cell binding agent through a linking group, and (B) a pharmaceutically acceptable carrier, diluent or excipient. A method for killing selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of a cytotoxic agent comprising one or more taxanes linked to a cell binding agent. Novel sulfur-containing taxanes.

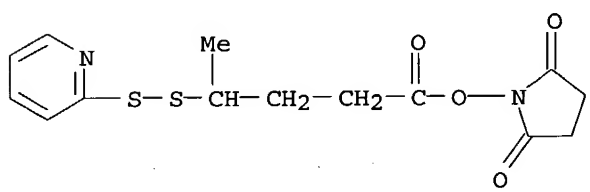
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **341498-08-6**
(reaction; cytotoxic taxane-cell-binding agent conjugates, and therapeutic use)
RN 341498-08-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



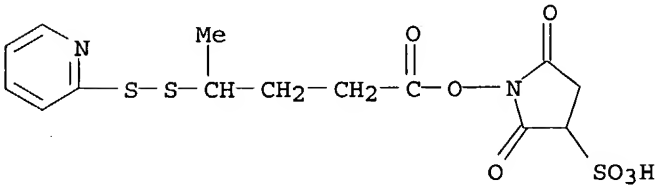
L37 ANSWER 4 OF 21 USPATFULL on STN
AN 2002:217411 USPATFULL
TI Methods for preparation of cytotoxic conjugates of maytansinoids and cell binding agents
IN Chari, Ravi V. J., Newton, MA, United States
Widdison, Wayne C., Somerville, MA, United States
PA Immunogen, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6441163 B1 20020827
AI US 2001-867598 20010531 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Kifle, Bruck
LREP Sughrue Mion, PLLC
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 962
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses a one-step process for the production of cytotoxic conjugates of maytansinoids and cell binding agents. Maytansinoids having a disulfide linker that bears a reactive moiety are linked to cell binding agents, such as antibodies, without prior modification of the cell binding agent. These conjugates are useful as therapeutic agents which are delivered specifically to target cells and are cytotoxic.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **341498-08-6P 452072-24-1P 452072-27-4P**
(process for preparation of cytotoxic conjugates of maytansinoid derivs. having a disulfide moiety and huN901 antibody)
RN 341498-08-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



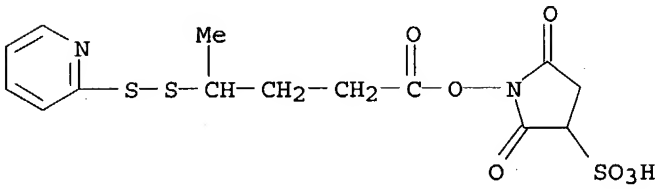
RN 452072-24-1 USPATFULL

CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]-, sodium salt (9CI) (CA INDEX NAME)



● Na

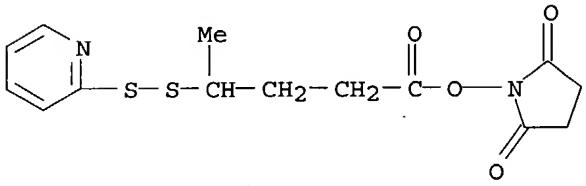
RN 452072-27-4 USPATFULL
CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 5 OF 21 USPATFULL on STN
AN 2002:165266 USPATFULL
TI CYTOTOXIC AGENTS COMPRISING TAXANES AND THEIR THERAPEUTIC USE
IN Chari, Ravi V. J., Newton, MA, UNITED STATES
Blattler, Walter A., Brookline, MA, UNITED STATES
PI US 2002086897 A1 20020704
US 6436931 B2 20020820
AI US 2002-59022 A1 20020130 (10)
RLI Division of Ser. No. US 2001-933018, filed on 21 Aug 2001, PATENTED
Division of Ser. No. US 2000-717026, filed on 22 Nov 2000, PATENTED
PRAI US 1999-167228P 19991124 (60)
DT Utility
FS APPLICATION
LREP SUGHRUE MION, PLLC, 2100 Pennsylvania Avenue, NW, Washington, DC, 20037-3213
CLMN Number of Claims: 44
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1283
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A cytotoxic agent comprising one or more taxanes linked to a cell binding agent. A therapeutic composition for killing selected cell populations comprising: (A) a cytotoxic amount of one or more taxanes covalently bonded to a cell binding agent through a linking group, and (B) a pharmaceutically acceptable carrier, diluent or excipient. A method for killing selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of a cytotoxic agent comprising one or more taxanes linked to a cell binding agent. Novel sulfur-containing taxanes.

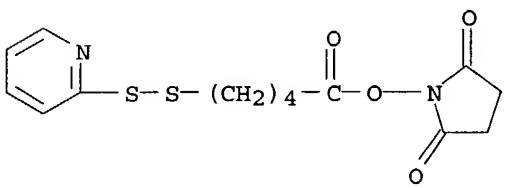
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **341498-08-6**
(reaction; cytotoxic taxane-cell-binding agent conjugates, and therapeutic use)
RN 341498-08-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



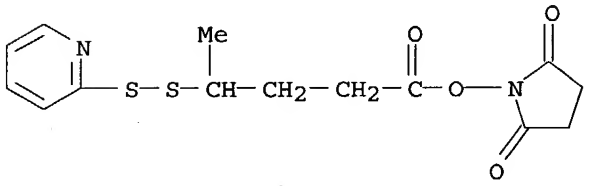
L37 ANSWER 6 OF 21 USPATFULL on STN
AN 2002:61898 USPATFULL
TI HER2-transgenic non-human tumor model
IN Erickson, Sharon, Hillsborough, CA, UNITED STATES
King, Kathleen, Pacifica, CA, UNITED STATES
Schwall, Ralph, Pacifica, CA, UNITED STATES
PI US 2002035736 A1 20020321
US 6632979 B2 20031014
AI US 2001-811115 A1 20010316 (9)
PRAI US 2000-189844P 20000316 (60)
DT Utility
FS APPLICATION
LREP KNOBBE MARTENS OLSON & BEAR LLP, 620 NEWPORT CENTER DRIVE, SIXTEENTH FLOOR, NEWPORT BEACH, CA, 92660
CLMN Number of Claims: 52
ECL Exemplary Claim: 1
DRWN 48 Drawing Page(s)
LN.CNT 2876
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns HER2-transgenic non-human mammals, animal models for screening drug candidates for the treatment of diseases and disorders associated with teh overexpression of HER2. In particular, the invention concerns animal models designed to test drug candidates for the treatment of HER2-overexpressing cancers, including breast cancer, that are not responding or poorly responding to current treatments.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **317331-86-5**
(humanized anti-ErbB2 antibody-maytansinoid conjugates and uses thereof in cancer therapy)
RN 317331-86-5 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-5-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 7 OF 21 USPATFULL on STN
AN 2002:22649 USPATFULL
TI Cytotoxic agents comprising taxanes and their therapeutic use
IN Chari, Ravi V.J., Newton, MA, UNITED STATES
Blattler, Walter A., Brookline, MA, UNITED STATES
PI US 2002013485 A1 20020131
US 6372738 B2 20020416
AI US 2001-933018 A1 20010821 (9)
RLI Division of Ser. No. US 2000-717026, filed on 22 Nov 2000, PENDING
PRAI US 1999-167228P 19991124 (60)
DT Utility
FS APPLICATION
LREP SUGHRUE, MION, ZINN, MACPEAK & SEAS, PLLC, 2100 Pennsylvania Avenue, NW, Washington, DC, 20037-3213
CLMN Number of Claims: 44
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1282
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A cytotoxic agent comprising one or more taxanes linked to a cell binding agent. A therapeutic composition for killing selected cell populations comprising: (A) a cytotoxic amount of one or more taxanes covalently bonded to a cell binding agent through a linking group, and (B) a pharmaceutically acceptable carrier, diluent or excipient. A method for killing selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of a cytotoxic agent comprising one or more taxanes linked to a cell binding agent. Novel sulfur-containing taxanes.

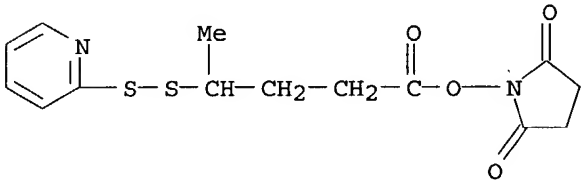
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **341498-08-6**
(reaction; cytotoxic taxane-cell-binding agent conjugates, and therapeutic use)
RN 341498-08-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 8 OF 21 USPATFULL on STN
AN 2002:14018 USPATFULL
TI Cytotoxic agents comprising taxanes and their therapeutic use
IN Chari, Ravi V. J., Newton, MA, United States
Blattler, Walter A., Brookline, MA, United States
PA Immunogen INC, Cambridge, MA, United States (U.S. corporation)
PI US 6340701 B1 20020122
AI US 2000-717026 20001122 (9)
PRAI US 1999-167228P 19991124 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Lambkin, Deborah C.; Assistant Examiner: D'Souza, Andrea M.
LREP Sughrue Mion, PLLC
CLMN Number of Claims: 24

ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1100
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A cytotoxic agent comprising one or more taxanes linked to a cell binding agent. A therapeutic composition for killing selected cell populations comprising: (A) a cytotoxic amount of one or more taxanes covalently bonded to a cell binding agent through a linking group, and (B) a pharmaceutically acceptable carrier, diluent or excipient. A method for killing selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of a cytotoxic agent comprising one or more taxanes linked to a cell binding agent. Novel sulfur-containing taxanes.

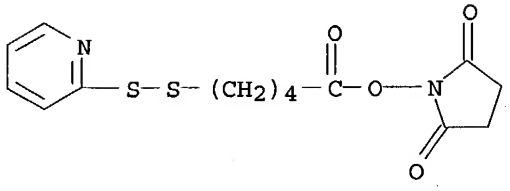
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **341498-08-6**
(reaction; cytotoxic taxane-cell-binding agent conjugates, and therapeutic use)
RN 341498-08-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 9 OF 21 USPATFULL on STN
AN 2002:3614 USPATFULL
TI Methods of treatment using anti-ErbB antibody-maytansinoid conjugates
IN Erickson, Sharon, Hillsborough, CA, UNITED STATES
Schwall, Ralph, Pacifica, CA, UNITED STATES
Sliwkowski, Mark, San Carlos, CA, UNITED STATES
PI US 2002001587 A1 20020103
AI US 2001-811123 A1 20010316 (9)
PRAI US 2000-238327P 20001005 (60)
US 2000-189844P 20000316 (60)
DT Utility
FS APPLICATION
LREP KNOBBE MARTENS OLSON & BEAR LLP, 620 NEWPORT CENTER DRIVE, SIXTEENTH FLOOR, NEWPORT BEACH, CA, 92660
CLMN Number of Claims: 54
ECL Exemplary Claim: 1
DRWN 46 Drawing Page(s)
LN.CNT 3898
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The application concerns methods of treatment using anti-ErbB receptor antibody-maytansinoid conjugates, and articles of manufacture suitable for use in such methods. In particular, the invention concerns ErbB receptor-directed cancer therapies, using anri-ErbB receptor antibody-maytansinoid conjugates.

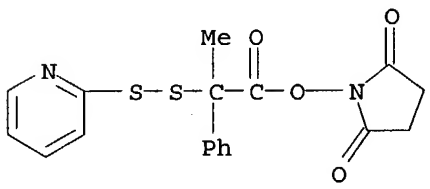
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **317331-86-5**
(humanized anti-ErbB2 antibody-maytansinoid conjugates and uses thereof in cancer therapy)
RN 317331-86-5 USPATFULL

CN 2,5-Pyrrolidinedione, 1-[[1-oxo-5-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 10 OF 21 USPATFULL on STN
AN 2000:119476 USPATFULL
TI Anti-aids immunotoxins
IN Kitto, George Barrie, Austin, TX, United States
PA Research Development Foundation, Carson City, NV, United States (U.S. corporation)
PI US 36866 20000912
US 5645836 19970708 (Original)
AI US 1998-109154 19980702 (9)
US 1995-422578 19950414 (Original)
DT Reissue
FS Granted
EXNAM Primary Examiner: Burke, Julie
LREP Adler, Benjamin Aaron
CLMN Number of Claims: 6
ECL Exemplary Claim: 4
DRWN 9 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 684
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a novel anti-AIDS immunotoxin. The immunotoxin comprises a toxin chemically conjugated to a monoclonal antibody directed against viral reverse transcriptase. Also provided are various methods of using this novel immunotoxin including methods of treating various diseases.

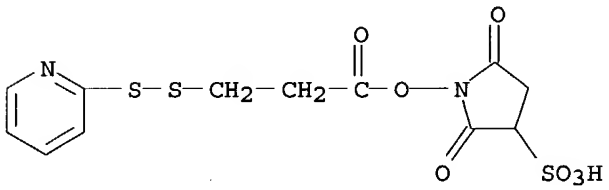
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **123266-19-3**
(conjugates of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
RN 123266-19-3 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-phenyl-2-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 11 OF 21 USPATFULL on STN
AN 1998:111628 USPATFULL
TI In vivo binding pair pretargeting
IN Pomato, Nicholas, Frederick, MD, United States
McCabe, Richard P., West Chester, PA, United States

Hawkins, Gregory Alan, Hastings, NE, United States
Bredehorst, Reinhard, Hamburg, Germany, Federal Republic of
Kim, Chong-Ho, Rockville, MA, United States
Vogel, Carl-Wilhelm Ernst, Hamburg, Germany, Federal Republic of
PA Akzo Nobel N.V., Arnhem, Netherlands (non-U.S. corporation)
PI US 5807534 19980915
AI US 1995-452938 19950530 (8)
RLI Continuation of Ser. No. US 1993-140186, filed on 4 Nov 1993, now patented, Pat. No. US 5578289 which is a continuation-in-part of Ser. No. US 1992-846453, filed on 4 Mar 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Green, Lora M.; Assistant Examiner: Musto, Neal A.
LREP Gormley, Mary E.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 1022
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for in-vivo targeting a functional moiety in a patient by administering a targeting moiety coupled to an affinity component, wherein the targeting moiety has affinity for binding sites in a target area, and administering a binding partner to the affinity component coupled to a functional moiety to localize the functional moiety in the target area. Preferably the targeting moiety is an antibody and the functional moiety is a radiometal when performing in vivo imaging or therapy. The affinity component may be a novel methotrexate analog.

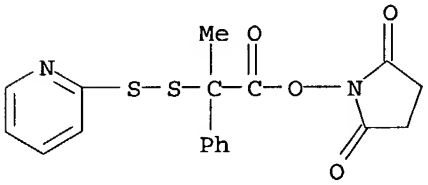
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **121115-30-8DP**, reaction products with antitumor monoclonal antibody and with dihydrofolate reductase
(preparation of and site-specific delivery of methotrexate-DTPA-indium-111 complex with)
RN 121115-30-8 USPATFULL
CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[1-oxo-3-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 12 OF 21 USPATFULL on STN
AN 97:58901 USPATFULL
TI Anti-AIDS immunotoxins
IN Kitto, George Barrie, Austin, TX, United States
PA Research Development Foundation, Carson City, NV, United States (U.S. corporation)
PI US 5645836 19970708
AI US 1995-422578 19950414 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Reeves, Julie E.
LREP Adler, Benjamin Aaron
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 8 Drawing Page(s)

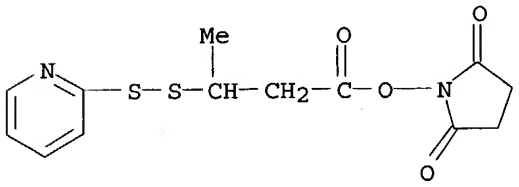
LN.CNT 672
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a novel anti-AIDS immunotoxin. The immunotoxin comprises a toxin chemically conjugated to a monoclonal antibody directed against vital reverse transcriptase. Also provided are various methods of using this novel including methods of treating various diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **123266-19-3**
(conjugates of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
RN 123266-19-3 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-phenyl-2-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)

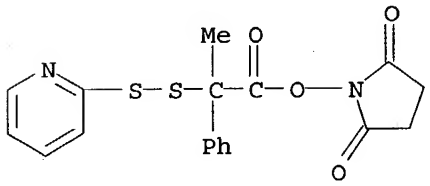


L37 ANSWER 13 OF 21 USPATFULL on STN
AN 92:92536 USPATFULL
TI Methods and compositions for the treatment of Hodgkin's disease
IN Thorpe, Philip, Ruislip, United Kingdom
Engert, Andreas, London, United Kingdom
PA Imperial Cancer Research Technology, London, United Kingdom (non-U.S. corporation)
PI US 5165923 19921124
AI US 1989-440050 19891120 (7)
DT Utility
FS Granted
EXNAM Primary Examiner: Nucker, Christine; Assistant Examiner: Kim, Kay K.
LREP Arnold, White & Durkee
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 2191
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods and compositions for the treatment of Hodgkin's disease and processes involving Hodgkin's disease cells or Reed-Sternberg cells, through specific elimination of Hodgkin's disease cells through the application of immunotoxin technology. The compositions of the invention include toxin conjugates composed of a Hodgkin's disease cell binding ligand conjugated to a toxin A chain moiety such as ricin A chain or deglycosylated ricin A chain, by means of a cross-linker or other conjugation which includes a disulfide bond. In preferred aspects of the invention, therapeutic amounts of conjugates composed of a CD-30 or IRac antibody or fragment thereof conjugated to deglycosylated A chain by means of an SMPT linker is administered to a Hodgkin's disease patient so as to specifically eliminate Hodgkin's disease cells without exerting significant toxicity against non-tumor cells. Also disclosed are particular hybridomas and monoclonal antibodies, and associated methodology, which may be employed, e.g., in the preparation of these immunotoxins as well as other uses such as diagnostic applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **107348-47-0 123266-19-3**
(linker, in preparation of immunotoxin conjugates, for Hodgkin's disease treatment)
RN 107348-47-0 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



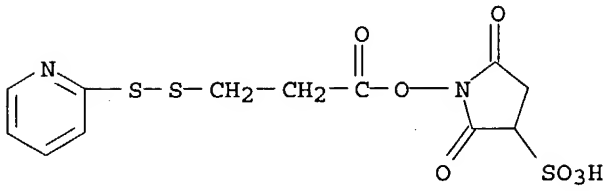
RN 123266-19-3 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-phenyl-2-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 14 OF 21 USPATFULL on STN
AN 90:4234 USPATFULL
TI Solubilization of proteins for pharmaceutical compositions using polyproline conjugation
IN Aldwin, Lois, San Mateo, CA, United States
Nitecki, Danute E., Berkeley, CA, United States
PA Cetus Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 4894226 19900116
AI US 1986-931197 19861114 (6)
DT Utility
FS Granted
EXNAM Primary Examiner: Hazel, Blondel
LREP McGarrigle, Philip L., Hasak, Janet E., Halluin, Albert P.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 966
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical composition is prepared wherein a biologically active conjugated protein is dissolved in an aqueous carrier medium in the absence of a solubilizing agent. The unconjugated protein, which is not readily water-soluble at pH 6-8 without such solubilizing agent, is covalently conjugated to polyproline via a flexible spacer arm and exhibits substantial biological activity.

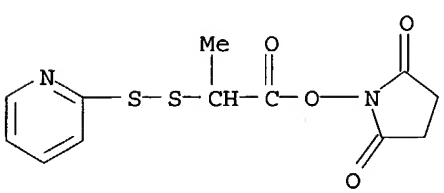
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **121115-30-8**
(reaction of, with polyproline)
RN 121115-30-8 USPATFULL
CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[1-oxo-3-(2-

pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)

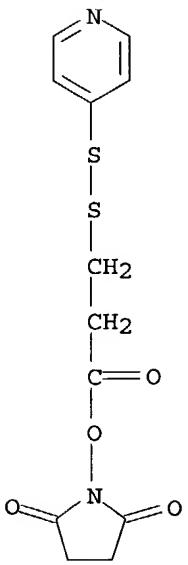


L37 ANSWER 15 OF 21 USPATFULL on STN
AN 86:823 USPATFULL
TI Pyridine compounds modifying proteins, polypeptides or polysaccharides
IN Carlsson, Jan P. E., Upsala, Sweden
Axen, Rolf E. A. V., Balinge, Sweden
Drevin, Hakan N. Y., Brunna, Sweden
Lindgren, Goran E. S., Almunge, Sweden
PA Pharmacia Fine Chemicals AB, Upsala, Sweden (non-U.S. corporation)
PI US 4563304 19860107
AI US 1984-582911 19840223 (6)
RLI Continuation of Ser. No. US 1981-238853, filed on 27 Feb 1981, now abandoned which is a continuation of Ser. No. US 1979-98302, filed on 28 Nov 1979, now abandoned which is a continuation of Ser. No. US 1978-946140, filed on 27 Sep 1978, now abandoned which is a division of Ser. No. US 1978-882546, filed on 2 Mar 1978, now patented, Pat. No. US 4149033
DT Utility
FS Granted
EXNAM Primary Examiner: Schain, Howard E.
LREP Philpitt, Fred
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 432
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel pyridine compounds having the formula R.sup.1 -S-S-A-Z are disclosed, in which formula R.sup.1 is 2-pyridyl, 5-nitro-2-pyridyl or 4-pyridyl, A is a hydrocarbon residue having 1-10 carbon atoms and Z is a group ##STR1## or acid addition salts of the last mentioned group, where n is 2 or 3, R.sup.1 has the same significance as R.sup.1 above and is equal thereto and R.sup.2 is methyl or ethyl. These compounds are particularly useful as bifunctional coupling agents and as thiolating agents.

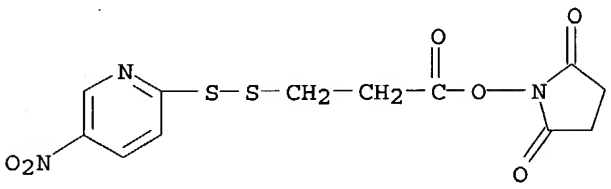
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **68617-67-4P 68617-68-5P 68617-69-6P**
(preparation of)
RN 68617-67-4 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



RN 68617-68-5 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(4-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



RN 68617-69-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[3-[(5-nitro-2-pyridinyl)dithio]-1-oxopropoxy]- (9CI) (CA INDEX NAME)



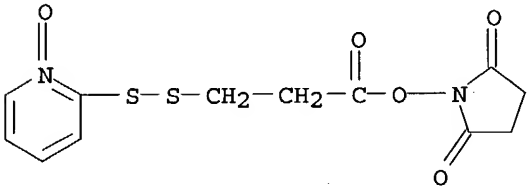
L37 ANSWER 16 OF 21 USPATFULL on STN
AN 81:16521 USPATFULL
TI Disulfide derivatives having S--S exchange reactivity
IN Fujii, Tadashiro, Mishima, Japan
Nakagawa, Nobuaki, Shizuoka, Japan
Kotani, Kikuo, Shizuoka, Japan
PA Toyo Jozo Kabushiki Kaisha, Shizuoka, Japan (non-U.S. corporation)
PI US 4258193 19810324
AI US 1979-57502 19790713 (6)
PRAI JP 1978-85900 19780713
DT Utility
FS Granted
EXNAM Primary Examiner: Jiles, Henry R.; Assistant Examiner: Whittenbaugh, Robert C.
LREP Young & Thompson
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 515
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A disulfide derivative, having S--S exchange reactivity, of the formula

R.sub.1 --S--S--R.sub.2 --CO--R.sub.3).sub.n R.sub.4 [I]

wherein R.sub.1 is 2-benzothiazolyl or 2-pyridyl-N-oxide, R.sub.2 is alkylene having optionally free or protected functional groups, R.sub.3 is the carboxyl residue of an amino acid or lower polypeptide, R.sub.4 is carboxyl or a reactive derivative thereof or protected carboxyl or imidate, and n is 0 or 1.

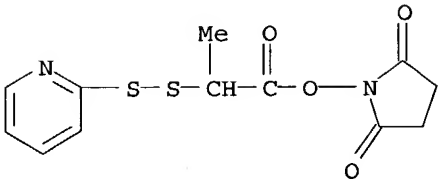
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **73919-78-5P**
(manufacture of, for use as exchange and cross-linking reagents for protein materials)
RN 73919-78-5 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[3-[(1-oxido-2-pyridinyl)dithio]-1-oxopropoxy]- (9CI) (CA INDEX NAME)



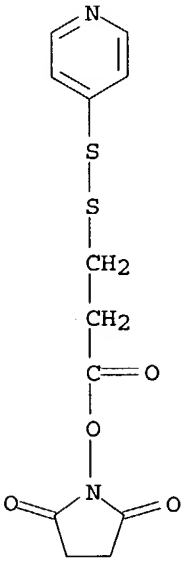
L37 ANSWER 17 OF 21 USPATFULL on STN
AN 79:18091 USPATFULL
TI Pyridine disulfide compounds
IN Carlsson, Jan P. E., Upsala, Sweden
Axen, Rolf E. A. V., Balinge, Sweden
Drevin, Hakan N. Y., Brunna, Sweden
Lindgren, Goran E. S., Almunge, Sweden
PA Pharmacia Fine Chemicals AB, Upsala, Sweden (non-U.S. corporation)
PI US 4149003 19790410
AI US 1978-882546 19780302 (5)
PRAI SE 1977-2462 19770304
DT Utility
FS Granted
EXNAM Primary Examiner: Trousof, Natalie; Assistant Examiner: Ramsuer, R. W.
LREP Philpitt, Fred
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 393
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel pyridine compounds having the formula R.sup.1 -S-S-A-Z are disclosed, in which formula R.sup.1 is 2-pyridyl, 5-nitro-2-pyridyl or 4-pyridyl, A is a hydrocarbon residue having 1-10 carbon atoms and Z is a group ##STR1## or acid addition salts of the last mentioned group, where n is 2 or 3, R.sup.1 has the same significance as R.sup.1 above and is equal thereto and R.sup.2 is methyl or ethyl. These compounds are particularly useful as bifunctional coupling agents and as thiolating agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **68617-67-4P 68617-68-5P 68617-69-6P**
(preparation of)
RN 68617-67-4 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-(2-pyridinyldithio)propoxy]- (9CI) (CA

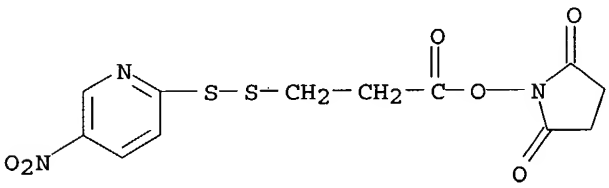
INDEX NAME)



RN 68617-68-5 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(4-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



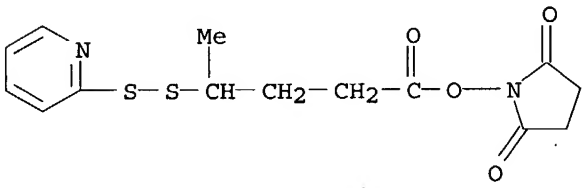
RN 68617-69-6 USPATFULL
CN 2,5-Pyrrolidinedione, 1-[3-[(5-nitro-2-pyridinyl)dithio]-1-oxopropoxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 18 OF 21 USPAT2 on STN
AN 2003:4169 USPAT2
TI Cytotoxic agents comprising taxanes and their therapeutic use
IN Chari, Ravi V. J., Newton, MA, United States
Blattler, Walter A., Brookline, MA, United States
PA Immunogen, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6706708 B2 20040316
AI US 2002-207814 20020731 (10)
RLI Division of Ser. No. US 2002-59022, filed on 30 Jan 2002, now patented,

Pat. No. US 6436931 Division of Ser. No. US 2001-933018, filed on 21 Aug 2001, now patented, Pat. No. US 6372738 Division of Ser. No. US 2000-717026, filed on 22 Nov 2000, now patented, Pat. No. US 6340701
PRAI US 1999-167228P 19991124 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Rotman, Alan L.; Assistant Examiner: Small, Andrea D.
LREP Sughrue Mion, PLLC
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1070
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A cytotoxic agent comprising one or more taxanes linked to a cell binding agent. A therapeutic composition for killing selected cell populations comprising: (A) a cytotoxic amount of one or more taxanes covalently bonded to a cell binding agent through a linking group, and (B) a pharmaceutically acceptable carrier, diluent or excipient. A method for killing selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of a cytotoxic agent comprising one or more taxanes linked to a cell binding agent. Novel sulfur-containing taxanes.

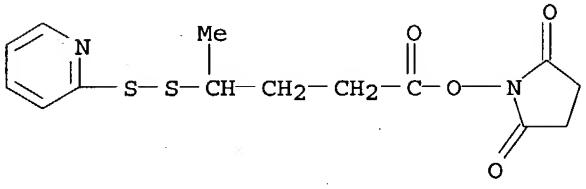
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **341498-08-6**
(reaction; cytotoxic taxane-cell-binding agent conjugates, and therapeutic use)
RN 341498-08-6 USPAT2
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 19 OF 21 USPAT2 on STN
AN 2002:165266 USPAT2
TI Cytotoxic agents comprising taxanes and their therapeutic use
IN Chari, Ravi V. J., Newton, MA, United States
Blattler, Walter A., Brookline, MA, United States
PA Immunogen Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6436931 B2 20020820
AI US 2002-59022 20020130 (10)
RLI Division of Ser. No. US 2001-933018, filed on 21 Aug 2001 Division of Ser. No. US 2000-717026, filed on 22 Nov 2000, now patented, Pat. No. US 6340701
PRAI US 1999-167228P 19991124 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Sololu, T. A.; Assistant Examiner: Small, Andrea D.
LREP Sughrue Mion, PLLC
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1092
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

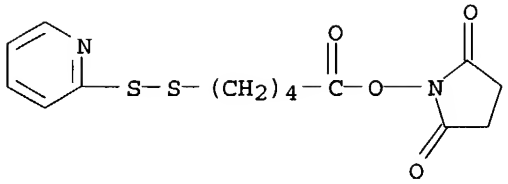
AB A cytotoxic agent comprising one or more taxanes linked to a cell binding agent. A therapeutic composition for killing selected cell populations comprising: (A) a cytotoxic amount of one or more taxanes covalently bonded to a cell binding agent through a linking group, and (B) a pharmaceutically acceptable carrier, diluent or excipient. A method for killing selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of a cytotoxic agent comprising one or more taxanes linked to a cell binding agent. Novel sulfur-containing taxanes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **341498-08-6**
(reaction; cytotoxic taxane-cell-binding agent conjugates, and therapeutic use)
RN 341498-08-6 USPAT2
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



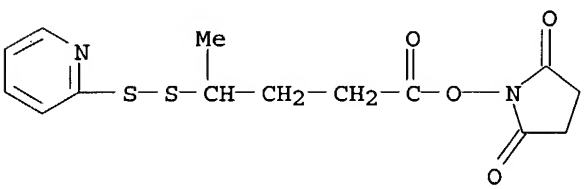
L37 ANSWER 20 OF 21 USPAT2 on STN
AN 2002:61898 USPAT2
TI Rodent HER2 tumor model
IN Erickson, Sharon, Hillsborough, CA, United States
King, Kathleen, Pacifica, CA, United States
Schwall, Ralph, Pacifica, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 6632979 B2 20031014
AI US 2001-811115 20010316 (9)
PRAI US 2000-189844P 20000316 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Crouch, Deborah; Assistant Examiner: Ton, Thalan N.
LREP Dreger, Esq., Ginger R., Heller Ehrman White & McAuliffe LLP
CLMN Number of Claims: 37
ECL Exemplary Claim: 1
DRWN 50 Drawing Figure(s); 48 Drawing Page(s)
LN.CNT 3009
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns HER2-transgenic non-human mammals, animal models for screening drug candidates for the treatment of diseases and disorders associated with the overexpression of HER2. In particular, the invention concerns animal models designed to test drug candidates for the treatment of HER2-overexpressing cancers, including breast cancer, that are not responding or poorly responding to current treatments.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **317331-86-5**
(humanized anti-ErbB2 antibody-maytansinoid conjugates and uses thereof in cancer therapy)
RN 317331-86-5 USPAT2
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-5-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L37 ANSWER 21 OF 21 USPAT2 on STN
AN 2002:22649 USPAT2
TI Cytotoxic agents comprising taxanes and their therapeutic use
IN Chari, Ravi V. J., Newton, MA, United States
Blatter, Walter A., Brookline, MA, United States
PA Immunogen Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6372738 B2 20020416
AI US 2001-933018 20010821 (9)
RLI Division of Ser. No. US 2000-717026, filed on 22 Nov 2000
PRAI US 1999-167228P 19991124 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Solola, T. A.; Assistant Examiner: Small, Andrea D'Souza
LREP Sughrue Mion, PLLC
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1107
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A cytotoxic agent comprising one or more taxanes linked to a cell binding agent. A therapeutic composition for killing selected cell populations comprising: (A) a cytotoxic amount of one or more taxanes covalently bonded to a cell binding agent through a linking group, and (B) a pharmaceutically acceptable carrier, diluent or excipient. A method for killing selected cell populations comprising contacting target cells or tissue containing target cells with an effective amount of a cytotoxic agent comprising one or more taxanes linked to a cell binding agent. Novel sulfur-containing taxanes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **341498-08-6**
(reaction; cytotoxic taxane-cell-binding agent conjugates, and therapeutic use)
RN 341498-08-6 USPAT2
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



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FILE COVERS 1907 - 15 Apr 2004 VOL 140 ISS 16
FILE LAST UPDATED: 14 Apr 2004 (20040414/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L38 31 (L1 OR L34)

=> d all hitstr tot l38

L38 ANSWER 1 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:162826 HCAPLUS
DN 140:217515
ED Entered STN: 29 Feb 2004
TI **Crosslinkers** with high reactivity and solubility and their use in the preparation of **conjugates** for targeted delivery of small molecule drugs
IN **Widdison, Wayne Charles**
PA **Immunogen, Inc., USA**
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004016801	A2	20040226	WO 2003-US22494	20030805 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004039176	A1	20040226	US 2003-633616	20030805 <--
PRAI US 2002-403652P	P	20020816 <--		

OS MARPAT 140:217515
AB Disclosed is a method of making **conjugates** of cell binding

agents and small mol. drugs comprising reacting a cell binding agent with a bifunctional **crosslinking** moiety to thereby provide the cell binding agent with a reactive disulfide group and then reacting the modified cell binding agent with a small mol. drug comprising a free thiol group. Bifunctional **crosslinking** moieties are also disclosed. For example, N-sulfosuccinimidyl 4-(5-nitro-2-pyridyldithio)-pentanoate was synthesized by esterifying 4-mercaptopentanoic acid converted from 1,3-dibromobutane with N-hydroxysulfosuccinimide, and then was effectively **conjugated** with murine monoclonal IgG1 N901 and maytansinoid DM1.

ST succinimidylpyridyldithiocarboxylate **crosslinker** prepn antibody cytotoxic **conjugate** targeted delivery

IT Immunoglobulins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(G1, monoclonal, N901, **conjugates** with disulfide **crosslinkers** and cytotoxic agents; preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT Antibodies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates**, with disulfide-containing **crosslinkers** and thiol-containing cytotoxic agents; preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT Antibodies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, **conjugates**, with disulfide-containing **crosslinkers** and thiol-containing cytotoxic agents; preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT Cytotoxic agents
Drug delivery systems
(preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT 138148-68-2, Maytansinoid DM 1
RL: RCT (Reactant); RACT (Reactant or reagent)
(Maytansinoid DM 1; preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT 138148-68-2DP, Maytansinoid DM 1, **conjugates** with IgG1 antibody N901 and disulfide **crosslinkers**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Maytansinoid DM 1; preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT 62-56-6, Thiourea, reactions 68-12-2, Dimethyl formamide, reactions 107-80-2, 1,3-Dibromobutane 1003-10-7, γ-Thiobutyrolactone 2127-03-9, 2,2'-Dipyridyl disulfide 2127-10-8, 2,2'-Dithiobis-(5-nitropyridine) 3772-13-2, Isobutylene sulfide 6066-82-6, N-Hydroxy succinimide 15658-35-2, 6,6'-Dithiodinicotinic acid 69866-21-3D, CC-1065, derivs. 82436-78-0D, N-Hydroxysulfosuccinimide, salts
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT 13095-73-3P, 4-Mercaptobutyric acid 125791-83-5P 131237-84-8P

140231-31-8P 250266-79-6P 663598-55-8P **663598-66-1DP**, salts
663598-78-5P 663598-96-7P 663599-02-8P 663599-04-0P 663599-09-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

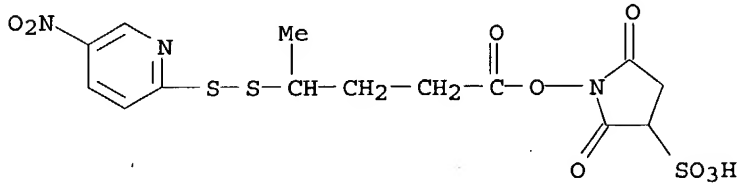
IT **663598-66-1DP**, salts, **conjugates** with IgG1 antibody and maytansinoid DM1
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT 1605-68-1D, Taxane, **conjugates** with disulfide **crosslinking** agents and antibodies 20830-81-3D, Daunorubicin, **conjugates** with disulfide **crosslinking** agents and antibodies 23214-92-8D, Doxorubicin, **conjugates** with disulfide **crosslinking** agents and antibodies 57103-68-1D, Maytansinol, **conjugates** with disulfide **crosslinking** agents and antibodies 69866-21-3D, CC-1065, **conjugates** with disulfide **crosslinking** agents and antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

IT **115088-06-7P 663598-61-6P 663598-85-4P**
663598-89-8DP, salts **663598-98-9P 663599-00-6DP**
, salts **663599-05-1P 663599-07-3DP**, salts
663599-10-8P 663599-11-9DP, salts
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** for **conjugating** with antibodies and small cytotoxic agents for targeted delivery)

IT **663598-66-1DP**, salts
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery)

RN 663598-66-1 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 1-[[4-[(5-nitro-2-pyridinyl)dithio]-1-oxopentyl]oxy]-2,5-dioxo- (9CI) (CA INDEX NAME)

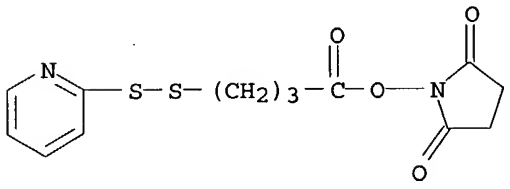


RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** and their **conjugates** with antibodies and small cytotoxic agents for targeted delivery

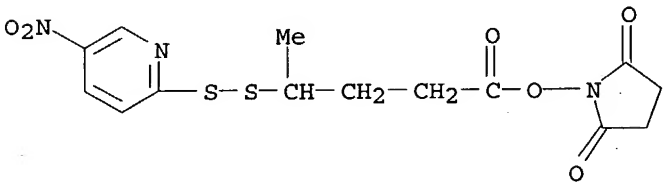
IT **115088-06-7P 663598-61-6P 663598-85-4P**
663598-89-8DP, salts **663598-98-9P 663599-00-6DP**
, salts **663599-05-1P 663599-07-3DP**, salts
663599-10-8P 663599-11-9DP, salts

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of succinimidylpyridyldithio carboxylic acid ester **crosslinkers** for **conjugating** with antibodies and small cytotoxic agents for targeted delivery)

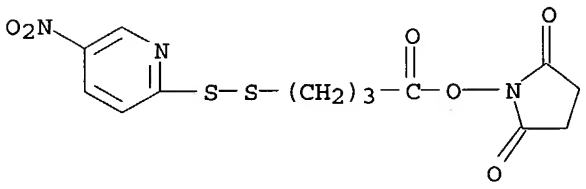
RN 115088-06-7 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-4-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



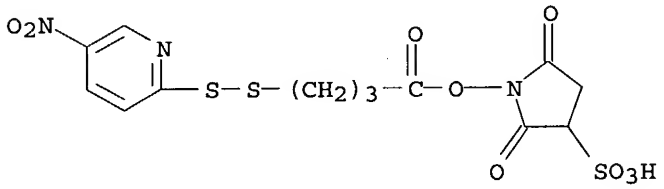
RN 663598-61-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[4-[(5-nitro-2-pyridinyl)dithio]-1-oxopentyl]oxy]- (9CI) (CA INDEX NAME)



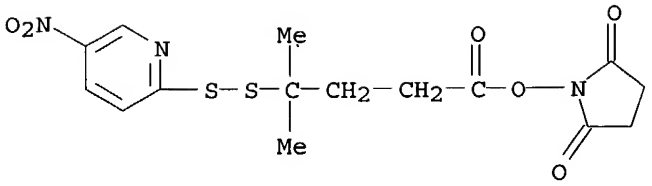
RN 663598-85-4 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[4-[(5-nitro-2-pyridinyl)dithio]-1-oxobutoxy]- (9CI) (CA INDEX NAME)



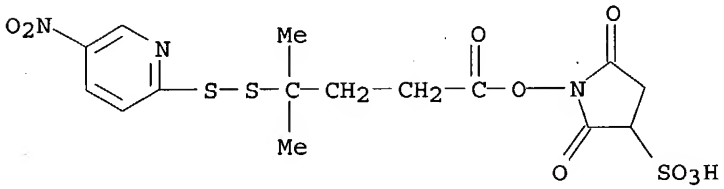
RN 663598-89-8 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 1-[4-[(5-nitro-2-pyridinyl)dithio]-1-oxobutoxy]-2,5-dioxo- (9CI) (CA INDEX NAME)



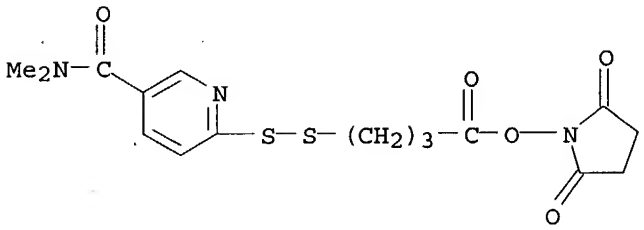
RN 663598-98-9 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[4-methyl-4-[(5-nitro-2-pyridinyl)dithio]-1-oxopentyl]oxy]- (9CI) (CA INDEX NAME)



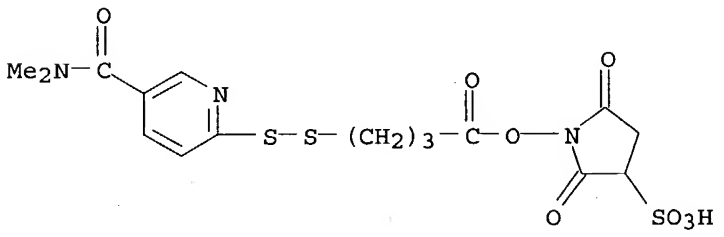
RN 663599-00-6 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 1-[[4-methyl-4-[(5-nitro-2-pyridinyl)dithio]-1-oxopentyl]oxy]-2,5-dioxo- (9CI) (CA INDEX NAME)



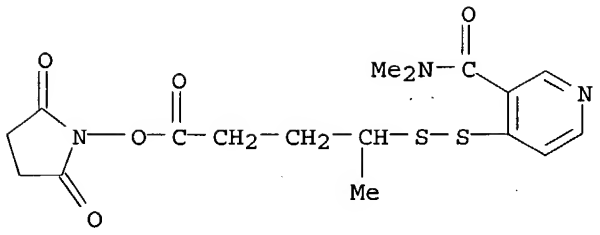
RN 663599-05-1 HCAPLUS
CN 3-Pyridinecarboxamide, 6-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutyl]dithio]-N,N-dimethyl- (9CI) (CA INDEX NAME)



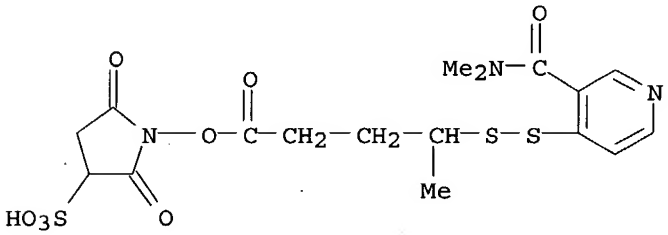
RN 663599-07-3 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 1-[4-[[5-[(dimethylamino)carbonyl]-2-pyridinyl]dithio]-1-oxobutoxy]-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 663599-10-8 HCAPLUS
CN 3-Pyridinecarboxamide, 4-[[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-methyl-4-oxobutyl]dithio]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 663599-11-9 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 1-[[4-[[3-[(dimethylamino)carbonyl]-4-pyridinyl]dithio]-1-oxopentyl]oxy]-2,5-dioxo- (9CI) (CA INDEX NAME)



L38 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:757853 HCAPLUS
DN 139:277123
ED Entered STN: 26 Sep 2003
TI A building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes
IN Gouliaev, Alex Haahr; Pedersen, Henrik; Thisted, Thomas; Lundorf, Mikkel Dybro; Sams, Christian; Franch, Thomas; Husemoen, Gitte Nystrup; Ho, Justin
PA Nuevolution A/s, Den.
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-10
CC 33-10 (Carbohydrates)
Section cross-reference(s): 3, 6, 27
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003078627	A2	20030925	WO 2003-DK177	20030314 <--
WO 2003078627	A3	20031231		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2002103008	A2	20021227	WO 2002-DK419	20020620 <--
WO 2002103008	A3	20031127		

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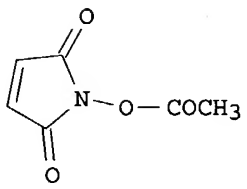
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	US 2004049008	A1	20040311	US 2002-175539	20020620 <--
PRAI	DK 2002-415	A	20020315 <--		
	US 2002-364056P	P	20020315 <--		
	US 2002-175539	A	20020620 <--		
	WO 2002-DK419	A	20020620 <--		
	US 2002-434439P	P	20021219		
	DK 2001-962	A	20010620 <--		
	US 2001-299443P	P	20010621 <--		

OS MARPAT 139:277123

GI



I

AB A building block having the dual capabilities of transferring the genetic information e.g. by recognizing an encoding element and transferring a functional entity to a recipient reactive group is disclosed. The building block can be designed with an adjustable transferability taking into account the components of the building block. The building block may be used in the generation of a single **complex** or libraries of different **complexes**, wherein the **complex** comprises an encoded mol. linked to an encoding element. Libraries of **complexes** are useful in the quest for pharmaceutically active compds. Thus, maleimide ester I was prepare and used in preparation of DNA.

ST nucleic acid hybridization library prepn DNA duplex synthon maleimide

IT Nucleic acid hybridization
Nucleic acid library
Synthons
(building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes)

IT DNA
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes)

IT DNA
RL: PNU (Preparation, unclassified); PREP (Preparation)
(double-stranded; building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes)

IT 23220-44-2P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes)

IT 607409-13-2P 607409-14-3P 607409-15-4P

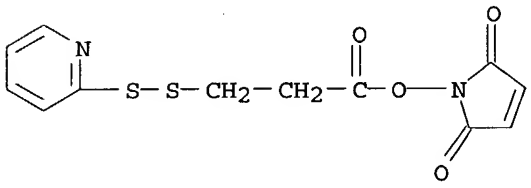
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes)

IT 75-36-5, Acetyl chloride 4814-74-8, N-Hydroxymaleimide
604799-80-6 604799-81-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes)

IT 606154-94-3 606154-95-4 606154-96-5 606154-97-6 606154-98-7
606154-99-8 606155-00-4 606155-01-5 606155-02-6 606983-51-1
RL: PRP (Properties)
(unclaimed sequence; building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes)

IT **604799-80-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(building block capable of functional entity transfer to nucleophile in preparation of DNA duplexes)

RN 604799-80-6 HCAPLUS
CN 1H-Pyrrole-2,5-dione, 1-[1-oxo-3-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:551336 HCAPLUS
DN 139:106431
ED Entered STN: 18 Jul 2003
TI Methods for preparing **immunoconjugates**
IN Mazzola, Gergory L.; Wang, William K.; Zapata, Gerardo A.
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-5 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003057163	A2	20030717	WO 2003-US205	20030102 <--
WO 2003057163	A3	20030918		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-345305P P 20020103 <--
AB Improved methods for preparing **immunoconjugates** are disclosed.

Conjugation of a maytansinoid to an antibody is exemplified.

ST maytansinoid **conjugation** antibody **immunoconjugate**

IT Antibodies
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates**; methods for preparing **immunoconjugates**)

IT Drug delivery systems
(**immunoconjugates**; methods for preparing **immunoconjugates**)

IT Disulfide group
Ion exchange chromatography
pH
(methods for preparing **immunoconjugates**)

IT Filtration
(tangential-flow filtration; methods for preparing **immunoconjugates**)

IT 1306-06-5, Hydroxyapatite 114752-67-9
RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(column; methods for preparing **immunoconjugates**)

IT **341498-08-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(linker; methods for preparing **immunoconjugates**)

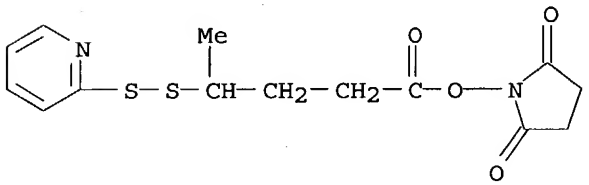
IT 35846-53-8DP, Maytansin, derivs., **conjugates** 139504-50-0DP, **conjugates**
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods for preparing **immunoconjugates**)

IT 75-05-8, Acetonitrile, uses 127-19-5, Dimethylacetamide
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; methods for preparing **immunoconjugates**)

IT **341498-08-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(linker; methods for preparing **immunoconjugates**)

RN 341498-08-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:880426 HCAPLUS

DN 138:100513

ED Entered STN: 21 Nov 2002

TI Tumor-Specific Novel Taxoid-Monoclonal Antibody **Conjugates**

AU Ojima, Iwao; Geng, Xudong; Wu, Xinyuan; Qu, Chuanxing; Borella, Christopher P.; Xie, Hongsheng; Wilhelm, Sharon D.; Leece, Barbara A.; Bartle, Laura M.; Goldmacher, Victor S.; Chari, Ravi V. J.

CS Department of Chemistry, State University of New York at Stony Brook, Stony Brook, NY, 11794-3400, USA

SO Journal of Medicinal Chemistry (**2002**), 45(26), 5620-5623
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society
DT Journal
LA English
CC 1-6 (Pharmacology)
AB Taxoids bearing methyldisulfanyl(alkanoyl) groups for taxoid-antibody **immunoconjugates** were designed, synthesized and their activities evaluated. A highly cytotoxic C-10 methyldisulfanylpropanoyl taxoid was **conjugated** to monoclonal antibodies recognizing the epidermal growth factor receptor (EGFR) expressed in human squamous cancers. These **conjugates** were shown to possess remarkable target-specific antitumor activity in vivo against EGFR-expressing A431 tumor xenografts in severe combined immune deficiency mice, resulting in complete inhibition of tumor growth in all the treated mice.
ST EGFR MAb **immunoconjugate** taxoid prepn antitumor
IT Drug delivery systems
(**immunoconjugates**; tumor-specific taxoid-MAb **conjugates** preparation)
IT Antibodies
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, **conjugates**; tumor-specific taxoid-MAb **conjugates** preparation)
IT Carcinoma
(squamous cell; tumor-specific taxoid-MAb **conjugates** preparation)
IT Antitumor agents
Human
(tumor-specific taxoid-MAb **conjugates** preparation)
IT Epidermal growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-specific taxoid-MAb **conjugates** preparation)
IT 485801-39-6DP, anti-EGFR MAb **conjugate** 485801-40-9P
485801-44-3P 485801-45-4P 485801-46-5P 485801-47-6P 485801-48-7P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tumor-specific taxoid-MAb **conjugates** preparation)
IT 178250-22-1
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(tumor-specific taxoid-MAb **conjugates** preparation)
IT 485801-35-2P 485801-36-3P 485801-38-5P 485801-50-1P 485801-51-2P
485801-52-3P 485801-55-6P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tumor-specific taxoid-MAb **conjugates** preparation)
IT 60033-23-0P 485801-37-4P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(tumor-specific taxoid-MAb **conjugates** preparation)
IT 115437-21-3 138148-59-1 178250-11-8 178250-16-3 181706-13-8
485801-49-8 485801-54-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(tumor-specific taxoid-MAb **conjugates** preparation)
IT 485801-53-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tumor-specific taxoid-MAb **conjugates** preparation)
IT **341498-08-6**
RL: RGT (Reagent); RACT (Reactant or reagent)
(tumor-specific taxoid-MAb **conjugates** preparation)
IT 485801-41-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(tumor-specific taxoid-MAb **conjugates** preparation)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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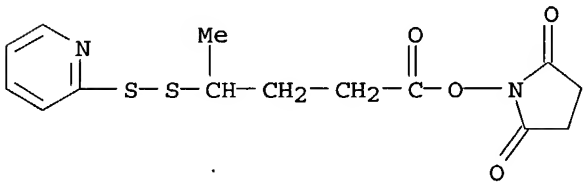
(32) Schiff, P; Nature 1979, V277, P665 HCAPLUS
(33) Sunada, H; Proc Natl Acad Sci U S A 1986, V83, P3825 HCAPLUS
(34) Vollmar, A; J Cell Physiol 1987, V131, P418 HCAPLUS
IT **341498-08-6**
RL: RGT (Reagent); RACT (Reactant or reagent)
(tumor-specific taxoid-MAb **conjugates** preparation)
RN 341498-08-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:655114 HCAPLUS
DN 137:201187
ED Entered STN: 29 Aug 2002
TI Process for preparation of cytotoxic **conjugates** of maytansinoids and cell binding agents
IN Chari, Ravi V. J.; **Widdison, Wayne C.**
PA **Immunogen, Inc., USA**
SO U.S., 17 pp.

CODEN: USXXAM
DT Patent
LA English
IC ICM C07D491-12
NCL 540458000
CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 34, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 6441163	B1	20020827	US 2001-867598	20010531	<--
	WO 2002098883	A1	20021212	WO 2002-US3378	20020214	<--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
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	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
	US 2003055226	A1	20030320	US 2002-161651	20020605	<--
PRAI	US 2001-867598	A	20010531	<--		
	WO 2002-US3378	W	20020214	<--		

OS CASREACT 137:201187; MARPAT 137:201187
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Maytansinoid derivs. having a disulfide linker, such as I [R1, R2 = H, Me, Et, alkyl; n = 1-5; X = reactive ester], were prepared The reactive ester group of I was reacted with cell binding agents, such as antibodies, to produce **conjugates.** These **conjugates** are useful as therapeutic agents which are delivered specifically to target cells and are cytotoxic. Thus, maytansinoid derivative II was prepared via a multistep synthetic sequence starting from 1,3-dibromobutane, sodium cyanide, thiourea, N-hydroxysuccinimide and N2'-deacetyl-N2'-[3-thiopropyl]-maytansine. II was reacted with huN901 antibody and purified over a Sephadex gel filtration to provide huN901-maytansinoid **conjugate** which was potent in killing antigen pos. cells, with an IC50 value of 1x10-10 M.

ST maytansinoid cell binding agent prepn; cytotoxicity maytansinoid antibody **conjugate** prepn

IT Antibodies
RL: RCT (Reactant); RACT (Reactant or reagent)
(huN901; process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT Drug delivery systems
(liposomes; process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT Cytotoxicity
(of **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT Disulfides
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(organic; process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pos. cells; process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT Antitumor agents
Human
Neoplasm
(process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT Gel permeation chromatography
(sephadex; for purification of **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT 452072-28-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antibody **conjugate**; process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT 452072-20-7P 452072-21-8P 452072-23-0P 452072-26-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT 51-28-5, 2,4-Dinitrophenol, reactions 62-56-6, Thiourea, reactions 88-75-5, 2-Nitrophenol 100-02-7, 4-Nitrophenol, reactions 107-80-2, 1,3-Dibromobutane 524-38-9, N-Hydroxyphthalimide 610-37-7, 3-Carboxy-4-nitrophenol 2127-03-9, 2,2'-Dithiodipyridine 6066-82-6, N-Hydroxysuccinimide 57103-68-1, Maytansinol 82436-78-0, N-Hydroxysulfosuccinimide 106627-54-7 115281-72-6 125672-65-3 139504-50-0 452072-29-6 452072-30-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

IT 125791-83-5P **341498-08-6P** 452072-22-9P **452072-24-1P** 452072-25-2P **452072-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

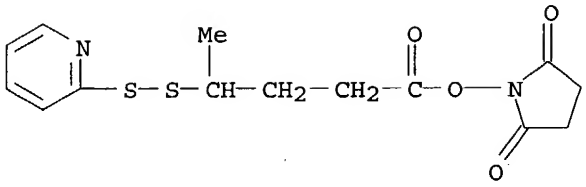
RE

(1) Chari; US 5208020 A 1993 HCAPLUS

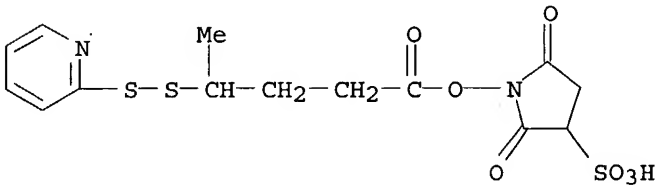
IT **341498-08-6P 452072-24-1P 452072-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of cytotoxic **conjugates** of maytansinoid derivs. having a disulfide moiety and huN901 antibody)

RN 341498-08-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)

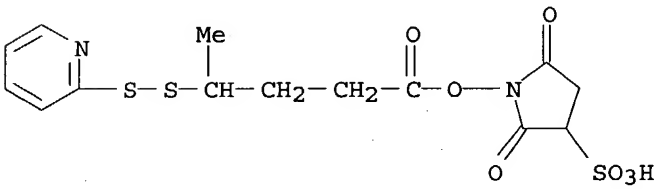


RN 452072-24-1 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]-, sodium salt (9CI) (CA INDEX NAME)



● Na

RN 452072-27-4 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:568348 HCAPLUS
DN 135:170778
ED Entered STN: 07 Aug 2001
TI Anti-tissue factor antibody-chemotherapeutic agent **conjugates**
IN Sekimori, Yasuo; Miyamoto, Hajime; Kawada, Hiromitsu; Nagao, Shunsuke
PA Chugai Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K045-00
ICS A61K039-395; A61K049-00; A61P035-00; C07K014-52; C07K014-745; C07K016-36; C07K019-00; C12P021-08
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001213804	A2	20010807	JP 2000-22898	20000131 <--

PRAI JP 2000-22898 20000131 <--

AB The invention relates to an anti-tissue factor antibody-antitumor agent **conjugate** or an anti-tissue factor antibody-toxin **conjugate** with a linking agent providing improved drug targeting effect. An immunotoxin of anti-tissue factor antibody-gelonin **conjugate** was prepared with N-succinimidyl 3-(2-pyridyldithio)propionate, and its inhibitory effect on protein synthesis in J 82 human bladder carcinoma cells was examined

ST **immunoconjugate** tissue factor antibody antitumor; immunotoxin tissue factor antibody gelonin

IT Ricins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ML-I (mistletoe lectin I); anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PAP-S (pokeweed antiviral protein); anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Tritin; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Volkesin; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Antitumor agents
Drug targeting
(anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Cytokines
Interferons
Interleukin 2
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(briodin; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dianthin 32; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT Pseudomonas
(endotoxin; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(endotoxins; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Drug delivery systems
(**immunoconjugates**; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Drug delivery systems
(immunotoxins; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Peptides, biological studies
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linking agents; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Drug delivery systems
(liposomes; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(luffin; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(momorcochin; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(momordins; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Antibodies
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(monoclonal; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(saporins; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Albumins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum, human, serum Albumin, linking agents; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxin A; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin

conjugates with linking agents)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trichokirin; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT 75037-46-6DP, Gelonin, **conjugates** with anti-tissue factor antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

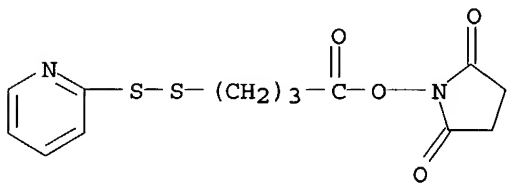
IT 9035-58-9, Blood-coagulation factor III
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT 50-07-7D, Mitomycin C, **conjugates** with anti-tissue factor antibodies 50-91-9D, 5-Fluoro-2'-deoxyuridine, **conjugates** with anti-tissue factor antibodies 54-62-6D, Aminopterin, **conjugates** with anti-tissue factor antibodies 57-22-7D, Vincristine, **conjugates** with anti-tissue factor antibodies 59-05-2D, Methotrexate, **conjugates** with anti-tissue factor antibodies 147-94-4D, Cytosine arabinoside, **conjugates** with anti-tissue factor antibodies 148-82-3D, Melphalan, **conjugates** with anti-tissue factor antibodies 316-46-1D, 5-Fluorouridine, **conjugates** with anti-tissue factor antibodies 9014-02-2D, Neocarzinostatin, **conjugates** with anti-tissue factor antibodies 11056-06-7D, Bleomycin, **conjugates** with anti-tissue factor antibodies 15663-27-1D, Cisplatinum, **conjugates** with anti-tissue factor antibodies 20830-81-3D, Daunorubicin, **conjugates** with anti-tissue factor antibodies 25316-40-9D, Adriamycin, **conjugates** with anti-tissue factor antibodies 33069-62-4D, Paclitaxel, **conjugates** with anti-tissue factor antibodies 41575-94-4D, Carboplatin, **conjugates** with anti-tissue factor antibodies 53643-48-4D, Vindesine, **conjugates** with anti-tissue factor antibodies 65988-88-7D, modeccin, **conjugates** with anti-tissue factor antibodies 95787-44-3D, Dodecandrin, **conjugates** with anti-tissue factor antibodies 114977-28-5D, Docetaxel, **conjugates** with anti-tissue factor antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT 58-85-5, Biotin 585-84-2, cis-Aconitic acid 6041-98-1, Glutamica cid dihydrazide 6539-14-6, 2-Iminothiolane 6953-60-2, S-Acetylmercaptosuccinic anhydride 9004-54-0, Dextran, biological studies 9044-05-7, Carboxymethyldextran 25322-68-3, Polyethylene glycol 37293-51-9, Aminodextran 58626-38-3 59012-54-3 68181-17-9, N-Succinimidyl 3-(2-pyridyldithio)propionate 79886-55-8 103708-10-7 103848-62-0 **115088-06-7** 115616-51-8 150244-18-1 158913-22-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linking agents; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)

IT 112263-86-2
RL: PRP (Properties)
(unclaimed protein sequence; anti-tissue factor antibody-chemotherapeutic agent **conjugates**)

IT **115088-06-7**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linking agents; anti-tissue factor antibody-antitumor agent **conjugates** or anti-tissue factor antibody-toxin **conjugates** with linking agents)
RN 115088-06-7 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-4-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:396857 HCAPLUS
DN 135:492
ED Entered STN: 01 Jun 2001
TI Cytotoxic agents comprising taxanes **conjugated** to cell-binding agents, and their therapeutic use
IN Chari, Ravi V.; Blattler, Walter A.
PA **Immunogen, Inc., USA**
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D305-14
ICS A61K039-395; C07K016-30; A61P035-00
CC 1-6 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	WO 2001038318	A1	20010531		WO 2000-US30149	20001121	<--
	W: AU, CA, JP, NZ						
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR						
	EP 1242401	A1	20020925		EP 2000-982077	20001121	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR						
	JP 2003514903	T2	20030422		JP 2001-540081	20001121	<--
	AU 765588	B2	20030925		AU 2001-19149	20001121	<--
	US 6340701	B1	20020122		US 2000-717026	20001122	<--
	US 2002013485	A1	20020131		US 2001-933018	20010821	<--
	US 6372738	B2	20020416				
	US 2002086897	A1	20020704		US 2002-59022	20020130	<--
	US 6436931	B2	20020820				
	US 2003004210	A1	20030102		US 2002-207814	20020731	<--
	US 6706708	B2	20040316				
PRAI	US 1999-167228P	P	19991124	<--			
	WO 2000-US30149	W	20001121	<--			
	US 2000-717026	A3	20001122	<--			
	US 2001-933018	A3	20010821	<--			
	US 2002-59022	A3	20020130	<--			

OS MARPAT 135:492
AB A cytotoxic agent is disclosed which comprises one or more taxanes (Markush included) linked to a cell-binding agent. A therapeutic composition

for killing selected cell populations comprises (a) a cytotoxic amount of one or more taxanes covalently bonded to a cell-binding agent through a linking group, and (b) a pharmaceutically acceptable carrier, diluent or excipient. A method for killing selected cell populations comprises contacting target cells or tissue containing target cells with an effective amount of a cytotoxic agent comprising one or more taxanes linked to a cell-binding agent. Sulfur-containing taxanes are also disclosed.

ST cytotoxic taxane cell binding agent **conjugate**; sulfur contg taxane cytotoxic **conjugate**

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and antibody fragments, **conjugates** with taxanes; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Epidermal growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to, taxane **conjugate**; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-erbB2; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Antitumor agents
(carcinoma, epidermoid, A431; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Growth factors, animal
Hormones, animal, biological studies
Interferons
Lymphokines
Transferrins
Vitamins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugates** with taxanes; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Antitumor agents
Cytotoxic agents
Drug delivery systems
Drug targeting
(cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Taxanes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

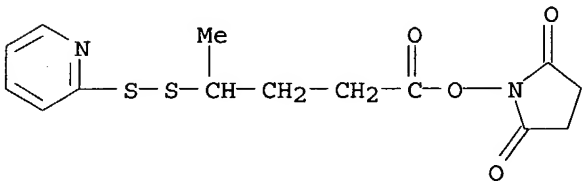
IT Antitumor agents
(mammary gland, SKBR3; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, **conjugates**, with taxanes; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Mammary gland
(neoplasm, inhibitors, SKBR3; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)

IT Sulfhydryl group
(thiol-containing taxanes; cytotoxic taxane-cell-binding agent

conjugates, and therapeutic use)
IT 62683-29-8D, Colony-stimulating factor, **conjugates** with taxanes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)
IT **341498-08-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Cetus Corp; WO 8912624 A 1989 HCAPLUS
(2) Chugai Pharmaceutical Co Ltd; WO 9925729 A 1999 HCAPLUS
(3) Chugai Pharmaceutical Co Ltd; EP 1033372 A 2000 HCAPLUS
(4) Neuromedica Inc; WO 9744026 A 1997 HCAPLUS
(5) Rothbard, J; WO 9852614 A 1998 HCAPLUS
(6) Safavy, A; JOURNAL OF MEDICINAL CHEMISTRY 1999, V42, P4919 HCAPLUS
(7) Squibb Bristol Myers Co; EP 0624377 A 1994 HCAPLUS
(8) Squibb Bristol Myers Co; WO 9819705 A 1998 HCAPLUS
(9) Uab Research Foundation; WO 0050059 A 2000 HCAPLUS
IT **341498-08-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; cytotoxic taxane-cell-binding agent **conjugates**, and therapeutic use)
RN 341498-08-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-4-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:12302 HCAPLUS
DN 134:91105
ED Entered STN: 05 Jan 2001
TI Humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy
IN Erickson, Sharon; Schwall, Ralph
PA Genentech, Inc., USA
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-48
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 15
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001000244	A2	20010104	WO 2000-US17229	20000623 <--
WO 2001000244	A3	20011004		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB,

GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT,
TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000012196 A 20020319 BR 2000-12196 20000623 <--
EP 1191944 A2 20020403 EP 2000-941649 20000623 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
JP 2003503365 T2 20030128 JP 2001-505951 20000623 <--
NZ 515975 A 20040130 NZ 2000-515975 20000623 <--
US 2002001587 A1 20020103 US 2001-811123 20010316 <--
US 2002035736 A1 20020321 US 2001-811115 20010316 <--
US 6632979 B2 20031014
PRAI US 1999-141316P P 19990625 <--
US 2000-189844P P 20000316 <--
WO 2000-US17229 W 20000623 <--
US 2000-238327P P 20001005 <--

AB The application concerns methods of treatment using anti-ErbB receptor antibody-maytansinoid **conjugates**, and articles of manufacture suitable for use in such methods. In particular, the invention concerns ErbB receptor-directed cancer therapies, using anti-ErbB receptor antibody-maytansinoid **conjugates**. The present invention is based on the unexpected exptl. finding that HERCEPTIN-maytansinoid **conjugates** are highly effective in the treatment of HER2 (ErbB2) overexpressing tumors that do not respond, or respond poorly, to HERCEPTINρ therapy. In one aspect, the present invention concerns a method for the treatment of a tumor in a mammal, wherein the tumor is characterized by the overexpression of an ErbB receptor and does not respond or responds poorly to treatment with a monoclonal anti-ErbB antibody, comprising administering to the mammal a therapeutically effective amount of a **conjugate** of the anti-ErbB antibody with a maytansinoid. The maytansinoid used in the **conjugates** of the present invention may be maytansine or, preferably, maytansinol or a maytansinol ester. The antibody and maytansinoid may be **conjugated** by a bispecific chemical linker,such as N-succinimidyl-4-(2-pyridylthio)propanoate (SPDP) or N-succinimidyl-4-(2-pyridylthio)pentanoate (SPP). Thelinking group between the antibody and the maytansinoid may, for example, be a disulfide, thioether, acid labile,photolabile, peptidase labile, or esterase labile group. In another aspect, the invention concerns an article of manufacture comprising a container and a composition contained therein, wherein the composition comprises an anti-ErbB antibody-maytansinoid **conjugate**, and further comprising a package insert or label indicating that the composition can be used to treat cancer characterized by overexpression of an ErbB receptor, preferably at a 2+ level or above.

ST antibody ErbB2 maytansinoid **conjugate** cancer therapy

IT Esters, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(C-3 ester of maytansinol, for **conjugation** with anti-ErbB2 antibodies; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Drugs
(EGF receptor-targeting, comprising anti-ErbB2 antibody **conjugated** with maytansinoid; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Drug resistance

(antitumor, to anti-ErbB antibody; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Disulfide group
(as chemical linker; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Thioethers
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as chemical linker; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Intestine, neoplasm
(colon, treatment of; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Intestine, neoplasm
(colorectal, treatment of; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Cytotoxic agents
(**conjugated** with anti-ErbB2 antibodies; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugates**, maytansinoid-; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Uterus, neoplasm
(endometrium, treatment of; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(erbB-3; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fragments, Fab; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heregulin, ErbB-4; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Antitumor agents
Drug targeting
Immunotherapy
(humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Epidermal growth factor receptors
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT Antibodies
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(humanized, huMAb4D5-1, huMAb4D5-2, huMAb4D5-3, huMAb4D5-4, huMAb4D5-5, huMAb4D5-6, huMAb4D5-7 and huMAb4D5-8 (HERCEPTIN); humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer

therapy)
IT Drug delivery systems
(**immunoconjugates**; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT Apoptosis
Cell death
(inducers of; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT Light
(labile, as chemical linker; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT Acids, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(labile, as chemical linker; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT Epitopes
(mapping; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT Antibodies
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, anti-ErbB2, growth inhibitory; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT Bladder
Mammary gland
Prostate gland
Salivary gland
(neoplasm, treatment of; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT Proliferation inhibition
(proliferation inhibitors, monoclonal antibody 4D5; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT Kidney, neoplasm
Lung, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Stomach, neoplasm
Thyroid gland, neoplasm
(treatment of; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT 180288-69-1, Herceptin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugated** with DM1; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT 35846-53-8, Maytansine 57103-68-1, Maytansinol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**conjugated** with anti-ErbB2 antibodies; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT 68181-17-9, SPDP **317331-86-5**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)
IT 9013-79-0, Esterase 9031-96-3, Peptidase
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(labile, as chemical linker; humanized anti-ErbB2 antibody-maytansinoid

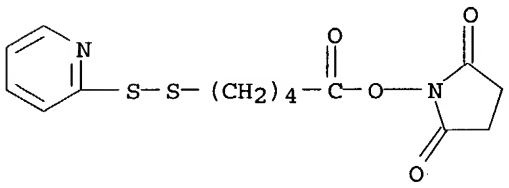
conjugates and uses thereof in cancer therapy)

IT 317863-81-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT 317863-82-4 317863-83-5 317863-84-6 317863-85-7 317863-86-8
317863-87-9 317863-88-0
RL: PRP (Properties)
(unclaimed protein sequence; humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

IT **317331-86-5**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(humanized anti-ErbB2 antibody-maytansinoid **conjugates** and uses thereof in cancer therapy)

RN 317331-86-5 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[[1-oxo-5-(2-pyridinyldithio)pentyl]oxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:828347 HCAPLUS
DN 135:367293
ED Entered STN: 28 Nov 2000
TI Synthesis of a non-viral vector for gene transfer via the high-affinity neurotensin receptor
AU Martinez-Fong, D.; Navarro-Quiroga, I.
CS Departamento de Fisiologia, Biofisica y Neurociencias;, Centro de Investigacion y de Estudios Avanzados del Instituto Politecnico Nacional de Mexico, Mexico City, 07000, Mex.
SO Brain Research Protocols (**2000**), 6(1,2), 13-24
CODEN: BRPRFP; ISSN: 1385-299X
PB Elsevier Science B.V.
DT Journal
LA English
CC 3-1 (Biochemical Genetics)
AB We describe herein a method for synthesizing a non-viral gene vector that exploits the internalization properties of neurotensin (NT), as well as the procedures for a successful gene transfer to cells via the high-affinity NT receptor. The gene vector is NT **cross-linked** with poly-l-lysine via N-succinimidyl-6-[3'-(2-pyridyldithio)propionamido]hexanoate (LC-SPDP). The SPDP-derivs. containing either NT or poly-L-lysine are purified by gel filtration. The non-viral vector resulting from the reaction of NT-SPDP with HS-SPDP-poly-L-lysine is purified on Biogel A-1.5 m. This vector is **complexed** with plasmid DNA at a specific molar ratio to form the NT-polyplex, which ensures the delivery of the gene of interest to cells under conditions of receptor-mediated internalization. The NT-polyplex has shown ability to mediate transient gene expression in vitro [Brain Res. Mol. Brain Res. 69 (1999) 249] and in vivo [Society Neurosci. Abstract 25 (1999) 67.7]. This approach holds great promise for research and therapy.
ST neurotensin polylysine **conjugate** plasmid **complex**

transformation; succinimidyl pyridyldithiopropionamidohexanoate **crosslinking** polylysine neurotensin vector gene transfer

IT Biological transport
(internalization, receptor-mediated; synthesis of a non-viral vector for gene transfer via the high-affinity neurotensin receptor)

IT Plasmids
(non-viral vector **complexed** with; synthesis of a non-viral vector for gene transfer via the high-affinity neurotensin receptor)

IT Gene therapy
Transformation, genetic
(synthesis of a non-viral vector for gene transfer via the high-affinity neurotensin receptor)

IT Neurotensin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(synthesis of a non-viral vector for gene transfer via the high-affinity neurotensin receptor)

IT 25104-18-1D, Poly-L-Lysine, **conjugates** with neurotensin
38000-06-5D, Poly-L-Lysine, **conjugates** with neurotensin
39379-15-2D, Neurotensin, **conjugates** with polylysine
RL: BUU (Biological use, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis of a non-viral vector for gene transfer via the high-affinity neurotensin receptor)

IT **374562-85-3DP**, reaction products with neurotensin and polylysine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of a non-viral vector for gene transfer via the high-affinity neurotensin receptor)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

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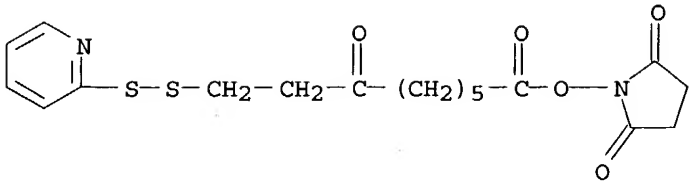
IT **374562-85-3DP**, reaction products with neurotensin and polylysine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of a non-viral vector for gene transfer via the high-affinity neurotensin receptor)

RN 374562-85-3 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[[1,7-dioxo-9-(2-pyridinyldithio)nonyl]oxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:564121 HCAPLUS
DN 132:20193
ED Entered STN: 08 Sep 1999
TI Bridging Group Effects on Nearest-Neighbor Recognition within Fluid Phospholipid Membranes
AU Tokutake, Nobuya; Miyake, Yasuhito; Regen, Steven L.
CS Department of Chemistry and Zettlemoyer Center for Surface Studies, Lehigh University, Bethlehem, PA, 18015, USA
SO Langmuir (**2000**), 16(1), 81-86
CODEN: LANGD5; ISSN: 0743-7463
PB American Chemical Society
DT Journal
LA English
CC 6-3 (General Biochemistry)
Section cross-reference(s): 26
AB The effects that the bridging group has on nearest-neighbor recognition (NNR) in phospholipid membranes (i.e., the thermodn. preference for homodimer formation) have been examined using a homologous series of dimers derived from 1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine (DMPE) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine (DSPE). When 3,3'-dithiodipropionyl (DTDP) was used as the exchangeable bridge, a statistical mixture of dimers was formed. In contrast, the use of a bridge that contained two addnl. methylene units resulted in a significant level of NNR; further extension of the bridge by two methylene units produced an addnl. increase in NNR. While cholesterol was found to induce significant NNR in bilayers made from lipid dimers having the DTDP moiety, its effect in membranes having longer bridging units was negligible. A simple model that accounts for these observations is presented, which is based on geometric and packing considerations. Exptl. evidence in support of this model has been obtained from relative differences in the gel to liquid-crystalline phase transition temps. and also from relative differences in fluorescence depolarization of 1,6-diphenyl-1,3,5-hexatriene (DPH), which have been measured in lipid membranes containing "short" and "long" bridges. Tighter packing in bilayers derived from phospholipid dimers having the DTDP bridge, together with the absence of nearest-neighbor recognition, points toward more cylindrically shaped phospholipids, and ones that are well-suited for model membrane studies. Possible biol. implications of these findings are also briefly discussed.
ST bridging group effects phospholipid membrane; nearest neighbor recognition phospholipid membrane; phospholipid membrane lateral organization; phosphatidylethanolamine dimer prepn bridging disulfide
IT Membrane, biological
(bilayer; bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)
IT Membrane phase transition, biological
(gel to liquid-crystalline; bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)
IT Phosphatidylethanolamines, biological studies
Phospholipids, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or

chemical process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(synthetic disulfide bridged dimers; bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)

IT 5961-85-3, Tris(2-carboxyethyl)phosphine
RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)

IT 1003-10-7, γ-Thiobutyrolactone 2067-33-6, 5-Bromovaleric acid 2127-03-9, 2,2'-Dipyridyl disulfide 6066-82-6, N-Hydroxysuccinimide 28230-32-2, 3-Hydroxy-1,2,3-benzotriazin-4(3H)one
RL: RCT (Reactant); RACT (Reactant or reagent)
(bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)

IT 13095-73-3P 30247-98-4P **115088-06-7P** 250266-79-6P 250266-80-9P 250266-81-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)

IT 136424-99-2P 136425-00-8P 136425-01-9P 250266-73-0P 250266-74-1P 250266-75-2P 250266-76-3P 250266-77-4P 250266-78-5P
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(synthetic phosphatidylethanolamine dimer; bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD

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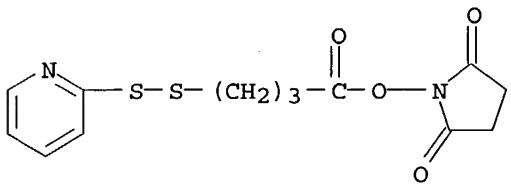
IT **115088-06-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bridging group effects on nearest-neighbor recognition within fluid phospholipid membranes)

RN 115088-06-7 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[1-oxo-4-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:169473 HCAPLUS

DN 128:229363

ED Entered STN: 21 Mar 1998

TI Anti-integrin α3 antibody **complexes**

IN Sekimori, Yasuo; Kawata, Hiromitsu; Tominaga, Eri; Hayakawa, Toru; Shimizu, Keiji

PA Chugai Seiyaku Kabushiki Kaisha, Japan

SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

IC ICM A61K039-395
ICS A61K045-00; A61K049-00; C07K016-30; C12P021-08; G01N033-53

CC 15-3 (Immunochemistry)
Section cross-reference(s): 1, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9809651	A1	19980312	WO 1997-JP3085	19970903 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9741344	A1	19980326	AU 1997-41344	19970903 <--
	JP 10130168	A2	19980519	JP 1997-252599	19970903 <--
PRAI	JP 1996-250887		19960903 <--		
	WO 1997-JP3085		19970903 <--		

AB **Complexes** comprising an anti-integrin α3 antibody or a fragment thereof having an antigen-binding capacity and a chemotherapeutic agent or toxin, and a medicinal composition containing the same. As the chemotherapeutic agent and toxin can efficiently be incorporated into

cells, particularly tumor cells by the internalization of the anti-integrin α3 antibody, the composition can exhibit cytocidal activities.

ST antibody integrin alpha3 chemotherapeutic antitumor toxin

IT Abrins
Ricins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Luffin; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ML-I (mistletoe lectin I); anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PAP (pokeweed antiviral protein); anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Antitumor agents
Chemotherapy
Protein sequences
Seed
(anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Antibodies
Cytokines
Interferons
Interleukin 2
Toxins
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(briodin; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dianthin 30; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria, A chain; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Toxins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(endotoxins, Pseudomonas; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Albumins, biological studies

Avidins
Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linker; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(momorcochin; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(momordins; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(saporins; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trichokirin; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tritin; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

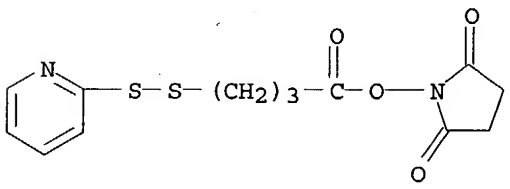
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α3; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT 204713-17-7 204713-19-9 204713-20-2 204713-22-4 204713-24-6
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT 50-07-7, Mitomycin C 50-91-9, 5-Fluoro-2'-deoxyuridine 54-62-6, Aminopterin 57-22-7, Vincristine 59-05-2, Methotrexate 147-94-4, Cytosine arabinoside 148-82-3, Melphalan 316-46-1, 5-Fluorouridine 9014-02-2, Neocarzinostatin 11056-06-7, Bleomycin 15663-27-1, cis-Platinum 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 25316-40-9, Adriamycin 41575-94-4, Carboplatin 53643-48-4, Vindesine 65988-88-7, Modeccin 75037-46-6, Gelonin 91933-11-8, Volkensin 95787-44-3, Dodecandrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)

IT 58-85-5, Biotin 110-05-4, DTBP 585-84-2, cis-Aconitic acid 6041-98-1, Glutamic acid, dihydrazide 6539-14-6, 2-Iminothiolane 6953-60-2, S-Acetyl mercaptosuccinic anhydride 9004-54-0, Dextran, biological studies 9044-05-7, Carboxymethyldextran 37293-51-9, Aminodextran 58626-38-3 68181-17-9, SPDP 79886-55-8 92921-26-1, Sulfo-SMPB 112241-19-7 **115088-06-7** 150244-18-1 158913-22-5 199804-25-6 204713-28-0 204713-29-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linker; anti-integrin α3 antibody **complexed** with

chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bristol-Myers Squibb Co; JP 06-501705 A 1994
(2) Bristol-Myers Squibb Co; EP 556285 A1 1994 HCAPLUS
(3) Bristol-Myers Squibb Co; WO 9207466 A1 1994 HCAPLUS
(4) Chugai Pharmaceutical Co Ltd; EP 729976 A1 1995 HCAPLUS
(5) Chugai Pharmaceutical Co Ltd; WO 9514041 A1 1995 HCAPLUS
(6) Chugai Pharmaceutical Co Ltd; JP 08-169900 A 1996 HCAPLUS
(7) Genentech Inc; JP 07-505528 A 1995
(8) Genentech Inc; US 5578704 A 1995 HCAPLUS
(9) Genentech Inc; US 562109 A 1995
(10) Genentech Inc; US 5652110 A 1995 HCAPLUS
(11) Genentech Inc; EP 633945 A1 1995 HCAPLUS
(12) Genentech Inc; WO 9320229 A1 1995 HCAPLUS
(13) Merck Patent Gmbh; JP 08-231597 A 1996 HCAPLUS
(14) Merck Patent Gmbh; EP 719859 A1 1996 HCAPLUS
(15) The Reagents Of The University Of Michigan; EP 282057 A1 1988 HCAPLUS
(16) The Reagents Of The University Of Michigan; JP 63-301833 A 1988 HCAPLUS
(17) The Reagents Of The University Of Michigan; CN 88102026 A 1988 HCAPLUS
IT **115088-06-7**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(linker; anti-integrin α3 antibody **complexed** with chemotherapeutic agent or toxin or cytokine for antitumor diagnosis and therapy)
RN 115088-06-7 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-4-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:694523 HCAPLUS
DN 125:326423
ED Entered STN: 25 Nov 1996
TI Novel anti-AIDS immunotoxins
IN Kitto, George Barrie
PA Research Development Foundation, USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K016-10
ICS C07K016-46; A61K039-42; A61K039-395; C12P021-08
CC 15-3 (Immunochemistry)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9632416	A1	19961017	WO 1996-US4996	19960411 <--

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,

TM, TT
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5645836	A	19970708	US 1995-422578	19950414	<--
ZA 9602911	A	19971013	ZA 1996-2911	19960101	<--
CA 2216210	AA	19961017	CA 1996-2216210	19960411	<--
AU 9655413	A1	19961030	AU 1996-55413	19960411	<--
AU 697418	B2	19981008			
EP 820470	A1	19980128	EP 1996-912684	19960411	<--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

CN 1184484	A	19980610	CN 1996-193981	19960411	<--
JP 11503730	T2	19990330	JP 1996-531175	19960411	<--
NZ 306768	A	20010330	NZ 1996-306768	19960411	<--
IL 117870	A1	20011223	IL 1996-117870	19960411	<--
RU 2191596	C2	20021027	RU 1997-118664	19960411	<--
US 36866	E	20000912	US 1998-109154	19980702	<--
PRAI US 1995-422578	A	19950414	<--		
WO 1996-US4996	W	19960411	<--		

AB The present invention provides a novel anti-AIDS immunotoxin. The immunotoxin comprises a toxin chemical **conjugated** to a monoclonal antibody directed against viral reverse transcriptase. The toxin is selected from pokeweed antiviral protein, gelonin, ricin, abrin, modeccin, dodecandrin, saporin, volkensin and vicumin. The **conjugates** is linked through **crosslinking** agent such as m-maleimidobenzoyl-N-hydroxysuccinimide, SPDP, α-iminothiolane hydrochloride, Me 3-mercaptopropionimidate, SMCC, 4-succinimidyloxycarbonyl-α-methyl-α-(2-pyridydithio)-toluene, N-succinimidyl(4-iodoacetyl)aminobenzoate, and sulfosuccinimidyl 4-(p-maleimidophenyl)butyrate. Also provided are various methods of using this novel immunotoxin including methods of treating various diseases. Monoclonal antibody to recombinant HIV-1 reverse transcriptase was prepared and **conjugated** with pokeweed antiviral protein as immunotoxin for AIDS.

ST monoclonal antibody recombinant HIV1 reverse transcriptase; toxin monoclonal antibody **conjugate** AIDS HIV

IT Abrins
Ricins
Toxins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugate**; **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)

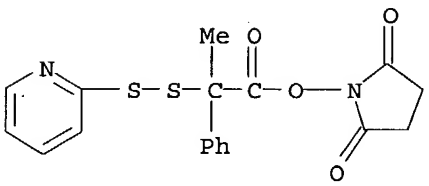
IT Acquired immune deficiency syndrome
(**conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)

IT Toxins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ML-I (mistletoe lectin I), **conjugate**; **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)

IT Proteins, specific or class
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PAP (pokeweed antiviral protein), **conjugate**; **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)

IT Virus, animal
(human immunodeficiency, **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS

immunotoxins)
IT Virus, animal
(human immunodeficiency 1, **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
IT Toxins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(immuno-, **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
IT Antibodies
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
IT Proteins, specific or class
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(saporins, **conjugate**; **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
IT 9068-38-6P, Reverse transcriptase
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HIV-1; **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
IT 65988-88-7P, Modeccin 75037-46-6P, Gelonin 91933-11-8P, Volkensin 95787-44-3P, Dodecandrin
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**conjugate**; **conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
IT 4781-83-3 64202-52-4 64987-85-5, SMCC 66592-92-5 68181-17-9, SPDP 103708-10-7 106145-13-5 **123266-19-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
IT **123266-19-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**conjugates** of monoclonal antibody to recombinant HIV-1 reverse transcriptase and toxin as anti-AIDS immunotoxins)
RN 123266-19-3 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-phenyl-2-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)

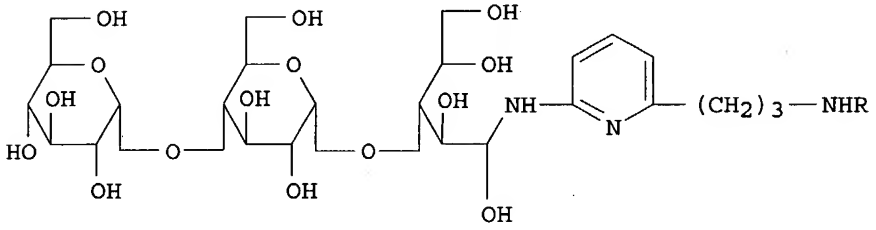


L38 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:95021 HCAPLUS
DN 124:146737
ED Entered STN: 15 Feb 1996

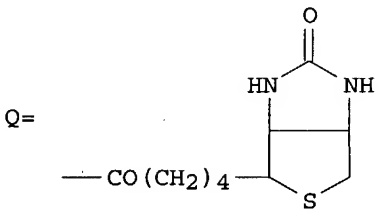
TI Method for fluorescent labeling of sugars and preparation of **complex** carbohydrates
IN Kusumoto, Shoichi; Fukase, Koichi
PA Seikagaku Kogyo Co Ltd, Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07H001-00
ICS C07H015-26; G01N021-78; G01N033-58
CC 33-7 (Carbohydrates)
Section cross-reference(s): 9
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 07252288	A2	19951003	JP 1994-41545	19940311 <--
PRAI JP 1994-41545		19940311 <--		

OS CASREACT 124:146737
GI



I



AB A fluorescent labeling method involves reductive amination of a sugar compound having at least a reducing sugar terminus with a 2-aminopyridine derivative having a N-protected aminoalkyl at the 6-position followed by deprotection of the NH2 group. The preferred protective is a urethane or haloacetyl group and is deprotected under basic or acidic condition or by reduction, preferably using aqueous piperidine for the deprotection under basic condition. A preparation of a **complex** carbohydrate involves reductive amination of a sugar compound having at least a reducing sugar terminus with a 2-aminopyridine derivative having a N-protected aminoalkyl at the 6-position followed by N-deprotection to obtain the sugar-linked 2-amino-6-amino-alkylpyridine derivative, and reacting the amino group of the 6-aminoalkyl group of the latter compound with an organic compound having a functional group capable of linking to the amino group directly or via a spacer having a functional group (e.g CO2H) capable of linking to the amino group. Preferred organic group is a sugar, protein, peptide, amino acid, fat, nucleic acid, nucleotide, nucleoside, biotin, or synthetic polymer. Thus, 2-tritylamino-6-(3-trifluoroacetylaminopropyl)pyridine, obtained by reduction of 2-tritylamino-6-(2-cyanoethyl)pyridine with LiAlH4 to 2-tritylamino-6-(2-aminoethyl)pyridine followed by reaction with trifluoroacetic anhydride, was stirred in a 1:1 mixture of AcOH-MeOH to give, after silica gel chromatog. and converting the partial AcOH salt to

the free amine by extraction with aqueous saturated NaHCO3, 2-amino-6-(6-trifluoroacetylaminopropyl)pyridine. The latter compound (27.8 μmol) and 5.55 μmol maltotriose were heated in a sealed tube at 90° for 3 h, cooled, and after adding a solution of 6.55 mg BH3.Me2NH in 33.5 mL AcOH, heated at 80° for 1 h in the sealed tube to give, after HPLC purification using a Cosmosil 5C18AR column, maltotritol derivative (I; R = COCF3), which was treated with 1 M aqueous piperidine to give 100% I (R = H). The latter compound was condensed with biotin N-hydroxysuccinimide ester in 0.5% NaHCO3-DMF to give, after the similar HPLC purification, 65% the biotin-labeled maltotritol derivative I (R = Q).

ST fluorescent labeling sugar; **complex** carbohydrate prepn; aminopyridine reductive amination reducing sugar; biotin labeled maltotritol prepn; pyridine contg sugar prepn

IT Albumins, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(**conjugate** with aminopyridine-containing maltotritol; fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

IT Fluorescent substances
(fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

IT Carbohydrates and Sugars, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

IT Indicators
(fluorescent, fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

IT Amination
(reductive, fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

IT 50-99-7, D-Glucose, reactions 69-79-4, Maltose 407-25-0, Trifluoroacetic anhydride 1109-28-0, Maltotriose 13139-17-8, N-Benzyloxycarbonyloxysuccinimide 24424-99-5, Di-tert-butyl dicarbonate 35013-72-0, Biotin N-hydroxysuccinimide ester 141775-75-9 153140-27-3 **173273-32-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

IT 159106-74-8P 173273-19-3P 173273-20-6P 173273-21-7P 173273-22-8P 173273-23-9P 173273-24-0P 173273-25-1P 173273-26-2P 173273-27-3P 173273-28-4P 173273-29-5P 173273-30-8P 173273-31-9P 173273-33-1P 173273-34-2P, 2-Tritylamino-6-(3-aminopropyl)pyridine 173273-35-3P, 2-Tritylamino-6-(3-tert-butoxycarbonylaminopropyl)pyridine 173395-52-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

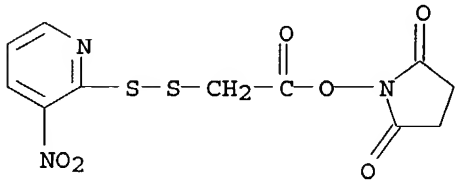
IT 159106-77-1DP, bovine serum albumin-bound 159106-78-2P 159106-79-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

IT **173273-32-0**

RL: RCT (Reactant); RACT (Reactant or reagent)
(fluorescent labeling of sugars by reductive amination of reducing sugars with aminopyridine derivative and preparation of **complex** carbohydrates containing aminopyridine)

RN 173273-32-0 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[[[(3-nitro-2-pyridinyl)dithio]acetyl]oxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:701187 HCAPLUS

DN 121:301187

ED Entered STN: 24 Dec 1994

TI Functional fluorescence labeling of carbohydrates and its use for preparation of **neoglycoconjugates**

AU Fukase, Koichi; Nakayama, Hideo; Kurosawa, Motohiro; Ikegaki, Toshiki; Kanoh, Takeshi; Hase, Sumihiro; Kusumoto, Shoichi

CS Fac. Sci., Osaka Univ., Osaka, 560, Japan

SO Journal of Carbohydrate Chemistry (**1994**), 13(5), 715-36
CODEN: JCACDM; ISSN: 0732-8303

DT Journal

LA English

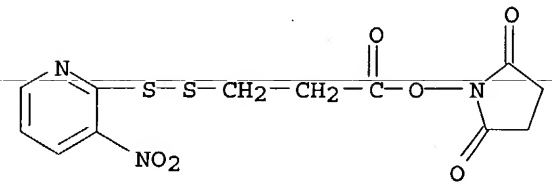
CC 33-7 (Carbohydrates)
Section cross-reference(s): 34, 41

AB New bifunctional reagents, 2-amino-6-carboxyethylpyridine and 2-amino-6-cyano-ethylpyridine, were designed and synthesized in order to provide a novel procedure for preparation of **neoglycoconjugates** from fluorescence-labeled and purified sugar chains. Labeling of model sugar chains with these reagents was effected by reductive amination using BH3·Me2NH to give corresponding 6-carboxyethylpyridylaminated (CEPA-) and 6-cyanotehylpyridylaminated (CNEPA-) derivs., which were readily purified by reversed phase HPLC. The reagent parts of the labeled products possess the functional groups which then serve as linkers for coupling with matrixes such as proteins and polymers. A CEPA-derivative of glucose was directly coupled with the ε-amino group of a Lys derivative to give a neoglycoprotein model. CNEPA-sugars were hydrogenated to give 6-aminopropylpyridylaminated (APPA-) derivs., which can then be readily used for the preparation of various types of **neoglycoconjugates** by use of appropriate spacers as exemplified by the coupling of APPA-maltotriose with bovine serum albumin (BSA), biotin, and acrylic acid. The reaction of APPAmaltotriose with succinimidyl 3-(3-nitro-2-pyridyldithio)propionate gave the corresponding amide to be used for a disulfide formation with BSA. Condensation with biotin was effected by use of N-hydroxysuccinimidobiotin. The **conjugation** of APPA-maltotriose with acrylic acid was carried out by use of 4-acryloyloxyphenyldimethylsulfonium methylsulfate to give the corresponding acrylamide, which can be used for the preparation of sugar-acrylamide copolymers.

ST fluorescence label amino sugar lysine; **neoglycoconjugate**; **glycoconjugate** neo; aminopyridine reductive amination sugar

IT Carbohydrates and Sugars, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(**conjugates**, **neoglycoconjugates**, preparation of)

IT Amination
(reductive, of sugars with 2-amino-6-carboxyethylpyridine and 2-amino-6-cyanoethylpyridine)
IT 153140-18-2P 153220-87-2P 159106-67-9P 159106-68-0P 159106-69-1P 159106-70-4P 159106-71-5P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and fluorescence of)
IT 5327-33-3P 23628-31-1P 26893-72-1P, 6-Acetamidopicolinic acid 69142-64-9P 153140-21-7P 153140-22-8P 153140-23-9P 153140-24-0P 153140-26-2P 153140-27-3P 159106-66-8P 159106-74-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of **neoglycoconjugates**)
IT 96386-87-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in synthesis of **neoglycoconjugates**)
IT 153140-16-0P 153140-17-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reductive amination by, of sugars in synthesis of **neoglycoconjugates**)
IT 159106-72-6P 159106-73-7P 159106-78-2P 159106-79-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 105-53-3, Diethyl malonate 1824-81-3 16640-68-9, Acetonitrile, (triphenylphosphoranylidene)- 23735-91-3 35013-72-0 141775-75-9 **159106-75-9** 159106-76-0 159106-77-1D, protein bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of **neoglycoconjugates**)
IT 107-96-0, 3-Mercaptopropionic acid 6066-82-6, N-Hydroxysuccinimide 68206-45-1, 3-Nitro-2-pyridinesulfenyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in synthesis of **neoglycoconjugates**)
IT **159106-75-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of **neoglycoconjugates**)
RN 159106-75-9 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[3-[(3-nitro-2-pyridinyl)dithio]-1-oxopropoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:665544 HCAPLUS
DN 119:265544
ED Entered STN: 25 Dec 1993
TI In vivo binding pair pretargeting for site-specific delivery of functional moiety in radioimaging or radiotherapy
IN Pomato, Nicholas; McCabe, Richard P.; Hawkins, Gregory A.; Brederhorst, Reinhard; Kim, Chong Ho; Vogel, Carl Wilhelm
PA AKZO N.V., Neth.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DT Patent
LA English
IC ICM A61K039-395
ICS A61K043-00; A61K049-00
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9317707	A1	19930916	WO 1993-US1858	19930303 <--
	W: AU, CA, FI, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9337368	A1	19931005	AU 1993-37368	19930303 <--
	AU 663582	B2	19951012		
	EP 590109	A1	19940406	EP 1993-906276	19930303 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 06507918	T2	19940908	JP 1993-515830	19930303 <--
	ZA 9303035	A	19931209	ZA 1993-3035	19930429 <--
	US 5578289	A	19961126	US 1993-140186	19931104 <--
PRAI	US 1992-846453		19920304 <--		
	WO 1993-US1858		19930303 <--		

AB A method for the in vivo targeting of a functional moiety in a patient (e.g. for imaging or therapy) comprises 1st administering a targeting moiety (e.g. antibody) coupled to an enzyme and thereafter administering a binding partner for the enzyme (e.g. enzyme inhibitor, enzyme substrate) coupled to a functional moiety forming an effector **complex** (preferably a radiometal **complex**), whereby the effector **complex** through the binding partner binds to the enzyme to localize the functional moiety in the target area. Recombinant human dihydrofolate reductase was **conjugated** with antitumor monoclonal antibody (MAb) 16.88 or with anti-human transferrin receptor MAb 5E9C11 via a heterobifunctional **crosslinker.** Methotrexate (a dihydrofolate reductase inhibitor) analog-DTPA (linked at the γ-carboxyl group of the glutamic acid) was prepared and chelated with 111In. The chelate bound to target cell-bound MAb-enzyme **conjugate.**

ST enzyme targeting agent **conjugate** radiometal **complex**; dihydrofolate reductase antitumor antibody **conjugate** imaging; methotrexate DTPA **conjugate** indium chelate targeting

IT Antibodies
Ligands
Receptors
RL: BIOL (Biological study)
(**conjugates** with enzyme, for site-specific delivery of enzyme-binding partner **conjugated** with functional group)

IT Toxins
RL: BIOL (Biological study)
(**conjugates** with enzyme-binding partner, site-specific delivery of, with enzyme-targeting agent **conjugates**)

IT Radiotherapy
(enzyme-binding radiometal **complex** site-specific delivery with enzyme-antibody **conjugate** in)

IT Pharmaceutical dosage forms
(of enzyme-targeting agent **conjugates**, for site-specific delivery of enzyme-binding partner **conjugated** with functional group)

IT Antigens
RL: BIOL (Biological study)
(CTAA 16-88 (colon tumor-associated antigen 16-88), monoclonal antibody to, **conjugates** with dihydrofolate reductase, for site-specific delivery of methotrexate-DTPA-indium-111 **complex**)

IT Radioelements, compounds

RL: BIOL (Biological study)
(**conjugates**, with enzyme-binding partner, site-specific delivery of, with enzyme-targeting agent **conjugates**)

IT Enzymes
RL: BIOL (Biological study)
(**conjugates**, with targeting agent, for site-specific delivery of enzyme-binding partner **conjugated** with functional group)

IT Radiography
(contrast agents, enzyme-binding radiometal **complex** and pretargeting enzyme-antibody **conjugate** as)

IT Pharmaceutical dosage forms
(**immunoconjugates**, of antibody and enzyme, for site-specific delivery of enzyme-binding partner **conjugated** with functional group)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, to tumor antigen or human transferrin receptor, **conjugates** with dihydrofolate reductase, for site-specific delivery of methotrexate-DTPA-indium-111 **complex**)

IT Transferrins
RL: BIOL (Biological study)
(receptors, monoclonal antibody to, **conjugates** with dihydrofolate reductase, for site-specific delivery of methotrexate-DTPA-indium-111 **complex**)

IT Receptors
RL: BIOL (Biological study)
(transferrin, monoclonal antibody to, **conjugates** with dihydrofolate reductase, for site-specific delivery of methotrexate-DTPA-indium-111 **complex**)

IT 9002-03-3D, Dihydrofolate reductase, monoclonal antibody **conjugates**
RL: BIOL (Biological study)
(for site-specific delivery of methotrexate-DTPA **complex** with indium-111, in imaging or therapy)

IT 15750-15-9DP, Indium-111, **complexes** with DTPA-methotrexate
151395-94-7DP, **complexes** with indium-111 151395-94-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and site-specific delivery of, with dihydrofolate reductase-monoclonal antibody **conjugate**)

IT 151395-95-8DP, photoactivated reaction products with dihydrofolate reductase
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and dihydrofolate reductase stabilization in relation to)

IT **121115-30-8DP**, reaction products with antitumor monoclonal antibody and with dihydrofolate reductase
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and site-specific delivery of methotrexate-DTPA-indium-111 **complex** with)

IT 151395-95-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, for stabilizing dihydrofolate reductase)

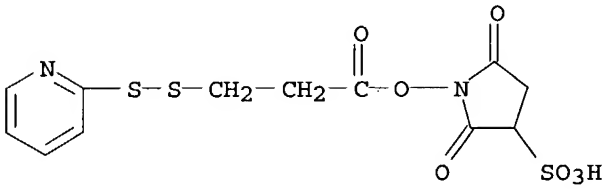
IT 79640-69-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with DTPA dianhydride)

IT 58775-35-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with NADP+)

IT 53-59-8, NADP+
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with azidonitrophenylaminopropionic acid)

IT 23911-26-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with methotrexate derivative)

IT 59-05-2D, Methotrexate, **conjugates** with radiometal
RL: BIOL (Biological study)
(site-specific delivery of, for imaging or therapy)
IT **121115-30-8DP**, reaction products with antitumor monoclonal antibody and with dihydrofolate reductase
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and site-specific delivery of methotrexate-DTPA-indium-111 **complex** with)
RN 121115-30-8 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[1-oxo-3-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:656534 HCAPLUS
DN 119:256534
ED Entered STN: 11 Dec 1993
TI **Immunoconjugates** for treatment of gastrointestinal tumors
IN Wright, Andrew Firman; Blakey, David Charles; Fitton, John edward; Lindholm, Leif; Lind, Peter; Holmgren, Jan
PA Imperial Chemical Industries PLC, UK; Kabi Pharmacia Ab
SO S. African, 118 pp.
CODEN: SFXXAB
DT Patent
LA English
IC ICM A61K
ICS C07K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	ZA 9204973	A	19930428	ZA 1992-4973	19920703 <--
	NO 9202383	A	19930104	NO 1992-2383	19920617 <--
	CA 2073113	AA	19930104	CA 1992-2073113	19920703 <--
	AU 9219430	A1	19930107	AU 1992-19430	19920703 <--
	AU 665546	B2	19960111		
	EP 528527	A2	19930224	EP 1992-306149	19920703 <--
	EP 528527	A3	19930317		
	EP 528527	B1	19980408		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	JP 05320065	A2	19931203	JP 1992-177212	19920703 <--
	HU 67048	A2	19950130	HU 1992-2219	19920703 <--
	HU 215243	B	19981130		
	AT 164768	E	19980415	AT 1992-306149	19920703 <--
	ES 2113923	T3	19980516	ES 1992-306149	19920703 <--
PRAI	GB 1991-14399	A	19910703 <--		

AB **Immunoconjugates** comprising a toxin moiety (e.g. recombinant ricin A chain) and a target cell-binding moiety (e.g. antibody C242) selective for gastrointestinal tumors, coupled by e.g. a bifunctional linker, thioether bond, or disulfide linkage, are useful for treatment of these tumors. Thus, recombinant ricin A was prepared in Escherichia coli by recombinant DNA technol. and coupled to mouse monoclonal antibody C242

(specific for human colorectal carcinoma cell line COLO 205) with N-succinimidyl 3-(2-pyridyldithio)butyrate as linker. The immunotoxin (2.0 mg/kg/day i.v. for 3 days) inhibited the growth of s.c. xenografts of COLO 205 cells in mice. An injection solution contained immunotoxin 1.0, NaOAc.3H2O 6.8, NaCl 7.2, and Tween 20 0.05 mg/mL.

ST ricin antibody **conjugate** gastrointestinal tumor; immunotoxin gastrointestinal tumor

IT Ricins
RL: PRP (Properties)
(A chains of, immunotoxin containing, for gastrointestinal tumor treatment)

IT Linking agents
(bifunctional, in immunotoxin preparation for gastrointestinal tumor treatment)

IT Deoxyribonucleic acid sequences
(for ricin A chain)

IT Gene, plant
RL: BIOL (Biological study)
(for ricin A chain, cloning and expression in Escherichia coli of)

IT Protein sequences
(of ricin A chain and monoclonal antibody to gastrointestinal tumor)

IT Plasmid and Episome
(pICI1187, ricin A chain gene on, cloning and expression in Escherichia coli of)

IT Antibodies
RL: BIOL (Biological study)
(to ricin A chain)

IT Deoxyribonucleic acid sequences
(complementary, for monoclonal antibody to gastrointestinal tumor)

IT Neoplasm inhibitors
(digestive tract, ricin A chain-containing immunotoxin)

IT Pharmaceutical dosage forms
(immunotoxins, ricin A chain-containing, for gastrointestinal tumor treatment)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, to gastrointestinal tumor, immunotoxin containing)

IT Digestive tract
(neoplasm, inhibitors, ricin A chain-containing immunotoxin)

IT 3976-69-0, Methyl (R)-3-hydroxybutyrate
RL: RCT (Reactant); RACT (Reactant or reagent)
(acid hydrolysis of)

IT 146315-53-9 146637-75-4, 1-141-Immunoglobulin G (mouse clone pKGE761 κ-chain anti-human antigen CA 242 reduced) 146637-79-8, 1-148-Immunoglobulin G (mouse clone pKGE762 γ-chain anti-human antigen CA 242 reduced)
RL: PRP (Properties)
(amino acid sequence of)

IT 151145-43-6 151145-44-7 151145-45-8 151145-46-9 151145-47-0 151145-48-1
RL: PRP (Properties)
(amino acid sequence of, in immunotoxin)

IT 6066-82-6, N-Hydroxysuccinimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, by pyridyldithiobutyric acid)

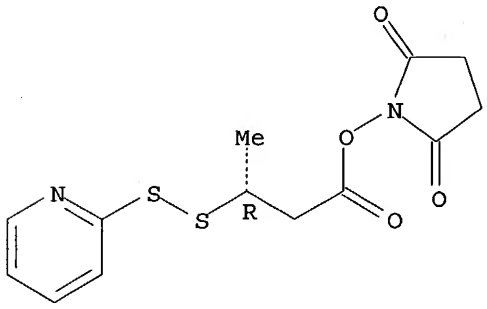
IT 26473-49-4D, 3-Mercaptobutyric acid, compds. with antibody and ricin A chain
RL: BIOL (Biological study)
(for gastrointestinal tumor treatment)

IT 146315-51-7 146637-73-2 146637-77-6
RL: PRP (Properties)
(nucleotide sequence of)

IT 2127-03-9, 2,2'-Dipyridyl disulfide
RL: RCT (Reactant); RACT (Reactant or reagent)

(oxidation of, with chlorine)
IT 625-72-9P, (R)-3-Hydroxybutyric acid
RL: PREP (Preparation)
(preparation and conversion to butyrolactone)
IT 151145-50-5P
RL: PREP (Preparation)
(preparation and esterification with hydroxysuccinimide)
IT 59089-57-5P, Pyridine-2-sulfenyl chloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with mercaptobutyric acid)
IT 115395-16-9P, (R)-3-Mercaptobutyric acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with pyridinesulfenyl chloride)
IT 65058-82-4P, (S)-β-Butyrolactone
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with thiolacetic acid)
IT **151145-49-2P**
RL: PREP (Preparation)
(preparation of, as linking agent for immunotoxin preparation)
IT **151145-49-2P**
RL: PREP (Preparation)
(preparation of, as linking agent for immunotoxin preparation)
RN 151145-49-2 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(2-pyridinyldithio)butoxy]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L38 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:534541 HCAPLUS
DN 119:134541
ED Entered STN: 02 Oct 1993
TI Biodistribution of anti-CEA F(ab')2 fragments **conjugated** with chelating polymers: influence of **conjugate** electron charge on tumor uptake and blood clearance
AU Slinkin, M. A.; Curtet, C.; Faivre-Chauvet, A.; Sai-Maurel, C.; Gestin, J. F.; Torchilin, V. P.; Chatal, J. F.
CS Lab. Biophys. Cancerol., INSERM, Nantes, 44035, Fr.
SO Nuclear Medicine and Biology (**1993**), 20(4), 443-52
CODEN: NMBIEO; ISSN: 0883-2897
DT Journal
LA English
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 14
AB F(ab')2 fragments of anti-carcinoembryonic antigen (CEA) monoclonal antibody (mAb) were modified with 3 chain-terminal polylysine-based

chelating polymers so as to carry different electron charges. Immunoreactive **conjugates** labeled with 111In up to a specific radioactivity of 120-140 μCi/μg were injected into nude mice bearing human colorectal carcinoma, and the biodistribution patterns were compared with each other and with that of an anti-CEA F(ab')2-DTPA control. **Immunoconjugate** modified with pos.-charged polymer produced the highest tumor uptake [up to 20% injected dose per g (ID/g)], with very significant nonspecific radioactivity in normal organs (particularly kidneys). When modified with a polymer carrying only a slight neg. charge, the **immunoconjugate** also produced fairly high tumor uptake (up to 18% ID/g), with much lower nonspecific radioactivity in normal organs. Highly neg.-charged **conjugate** produced the lowest tumor uptake (up to 8% ID/g), whereas blood and whole-body clearances were the fastest but slower than those of conventionally labeled F(ab')2 mAb. The possible mechanisms for the effects described are discussed.

ST indium 111 monoclonal antibody biodistribution imaging; chelating polymer indium 111 monoclonal antibody

IT Imaging
(immuno-, indium-111-labeled anti-carcinoembryonic antigen monoclonal antibody F(ab')2 fragment preparation and metabolism and biodistribution studies
in relation to)

IT Neoplasm, metabolism
(indium-111-anti-carcinoembryonic antigen monoclonal antibody F(ab')2 fragment distribution in, imaging in relation to)

IT Chelating agents
(polymers, anti-carcinoembryonic antigen monoclonal antibody F(ab')2 fragment **conjugation** with, for indium-111 labeling)

IT Intestine, neoplasm
(large, carcinoma, indium-111-anti-carcinoembryonic antigen monoclonal antibody F(ab')2 fragment distribution in, imaging in relation to)

IT Antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(monoclonal, **complexes**, with indium-111, preparation and metabolism and biodistribution of, tumor imaging in relation to)

IT Antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(monoclonal, indium-111-labeled F(ab')2 fragment of, to carcinoembryonic antigen, preparation and metabolism and biodistribution of, tumor imaging in relation to)

IT 23911-26-4D, reaction products with polylysine derivative and succinimidyldithiopropionate 67178-46-5D, acyl derivs., reaction products with succinimidyldithiopropionate and DTPA anhydride
67178-46-5D, reaction products with succinimidyldithiopropionate and DTPA anhydride **126144-47-6D**, reaction products with polylysine derivative and DTPA anhydride
RL: BIOL (Biological study)
(anti-carcinoembryonic antigen monoclonal antibody F(ab')2 fragments **conjugation** with, for indium-111 labeling)

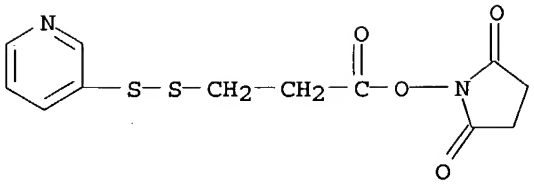
IT 15750-15-9DP, Indium-111, anti-carcinoembryonic antigen monoclonal antibodies labeled with, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and metabolism and biodistribution of, chelating polymers labeling
method and tumor imaging in relation to)

IT **126144-47-6D**, reaction products with polylysine derivative and DTPA anhydride
RL: BIOL (Biological study)
(anti-carcinoembryonic antigen monoclonal antibody F(ab')2 fragments **conjugation** with, for indium-111 labeling)

RN 126144-47-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(3-pyridinyldithio)propoxy]- (9CI) (CA

INDEX NAME)



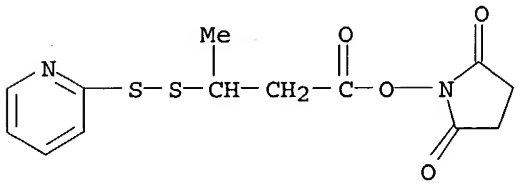
L38 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:32612 HCAPLUS
DN 118:32612
ED Entered STN: 03 Feb 1993
TI Molecular and biological properties of an abrin A chain immunotoxin designed for therapy of human small cell lung cancer
AU Wawrzynczak, E. J.; Zangemeister-Wittke, U.; Waibel, R.; Henry, R. V.; Parnell, G. D.; Cumber, A. J.; Jones, M.; Stahel, R. A.
CS Sect. Immunol., Inst. Cancer Res., Sutton/Surrey, SM2 5NG, UK
SO British Journal of Cancer (**1992**), 66(2), 361-6
CODEN: BJCAAI; ISSN: 0007-0920
DT Journal
LA English
CC 1-6 (Pharmacology)
AB An immunotoxin (IT) comprising abrin A chain attached to the mouse monoclonal antibody SWA11, recognizing a cell surface antigen highly associated with human small cell lung cancer (SCLC), was synthesized using a hindered disulfide **crosslinker**, N-succinimidyl-3-(2-pyridyldithio)butyrate (SPDB), and purified by Blue Sepharose CL-6B affinity chromatog. The IT preparation contained monomeric **conjugate**, composed of one abrin A chain mol. linked to one SWA11 mol., and was free from **unconjugated** A chain or antibody. The IT fully retained the cell-binding capacity of the antibody component and the ribosome-inactivating activity of the abrin A chain. In cytotoxicity assays using the SW2 SCLC cell line in tissue culture, the SWA11-SPDB-abrin A chain inhibited the incorporation of [3H]leucine by 50% at a concentration of 10 pM and by 99% at a concentration of 1 nM. The antitumor efficacy of the IT was tested in nude mice bearing established s.c. solid SW2 tumor xenografts. A single i.v. injection of the SWA11-SPDB-abrin A chain at a non-toxic dose induced a 7-10-day growth delay that could not be matched by equivalent doses of either **unconjugated** SWA11 or abrin A chain alone. Thus, the antigen recognized by SWA11 is an effective target for therapy of SCLC with A chain ITs in vivo.
ST abrin A chain immunotoxin lung cancer
IT Abrins
RL: SPN (Synthetic preparation); PREP (Preparation)
(**conjugates**, A chain, with monoclonal antibody, preparation of, as immunotoxin for therapy of human small cell lung cancer)
IT Pharmaceutical dosage forms
(immunotoxins, abrin A chain-monoclonal antibody **conjugates** preparation as, for therapy of human small cell lung cancer)
IT Neoplasm inhibitors
(lung small-cell carcinoma, abrin A chain-monoclonal antibody **conjugates** preparation as)
IT Antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(monoclonal, **conjugates**, with abrin A chain, preparation of, as immunotoxin for therapy of human small cell lung cancer)
IT Lung, neoplasm

(small-cell carcinoma, inhibitors, abrin A chain-monoclonal antibody **conjugates** preparation as)

IT **107348-47-0**
RL: BIOL (Biological study)
(abrin A chain immunotoxin preparation with, as hindered disulfide **crosslinker**)

IT **107348-47-0**
RL: BIOL (Biological study)
(abrin A chain immunotoxin preparation with, as hindered disulfide **crosslinker**)

RN 107348-47-0 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:578165 HCAPLUS
DN 117:178165
ED Entered STN: 01 Nov 1992
TI Enhanced stability of an immunotoxin made with abrin A chain and a hindered disulfide **crosslinker**
AU Cumber, Alan; Wawrzynczak, Edward
CS Inst. Cancer Res., Sutton, SM2 5NG, UK
SO Biochemical Society Transactions (**1992**), 20(4), 312S
CODEN: BCSTB5; ISSN: 0300-5127
DT Journal
LA English
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1
AB The enhanced stability in vivo of A chain immunotoxins constructed using a **crosslinker** that introduces a partially hindered disulfide bond is reflected in a greater resistance to splitting by reductive cleavage in vitro. The structure of abrin A chain can apparently also contribute to the stability of the disulfide linkage in vitro and in vivo. The effect of including the partially hindered **crosslinker** and the abrin A chain were additive in part and resulted in a more robust immunotoxin mol.
ST abrin A **crosslinked** immunotoxin stability; disulfide bond abrin immunotoxin stability
IT **Crosslinking** agents
(with hindered disulfide bond, stability of abrin A chain-containing immunotoxin in relation to)
IT Abrins
RL: BIOL (Biological study)
(A, of immunotoxin, stability of, **crosslinker** with hindered disulfide bond enhancement of)
IT Pharmaceutical dosage forms
(immunotoxins, abrin A chain-containing, stability of, **crosslinker** with hindered disulfide bond enhancement of)
IT Antibodies
RL: BIOL (Biological study)
(monoclonal, immunotoxins containing **crosslinked** abrin A chain and, stability of, disulfide bond in relation to)
IT Molecular structure-property relationship

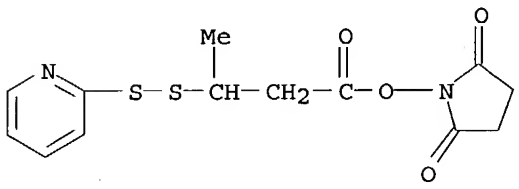
(stability, of abrin A chain-containing immunotoxin, **crosslinker** with hindered disulfide bond in relation to)

IT 68181-17-9, N-Succinimidyl-3-(2-pyridyldithio)propionate **107348-47-0**
RL: BIOL (Biological study)
(abrin A chain of immunotoxin **crosslinked** with, stability of, disulfide bond in relation to)

IT **107348-47-0**
RL: BIOL (Biological study)
(abrin A chain of immunotoxin **crosslinked** with, stability of, disulfide bond in relation to)

RN 107348-47-0 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:563351 HCAPLUS

DN 117:163351

ED Entered STN: 01 Nov 1992

TI Structural features of the antibody-A chain linkage that influence the activity and stability of ricin A chain immunotoxins

AU Cumber, Alan J.; Westwood, John H.; Henry, Raymond V.; Parnell, Geoffrey D.; Coles, Brian F.; Wawrzynczak, Edward J.

CS Sect. Immunol., Inst. Cancer Res., Sutton/Surrey, SM2 5NG, UK

SO Bioconjugate Chemistry **(1992)**, 3(5), 397-401
CODEN: BCCHES; ISSN: 1043-1802

DT Journal

LA English

CC 1-3 (Pharmacology)

AB The importance of the various structural elements constituting a ricin A chain immunotoxin to the stability of the disulfide bond between the antibody and A chain was examined using a panel of **immunoconjugates** prepared with the mouse monoclonal antibody Fib75. Analogs of the standard ricin A chain immunotoxin prepared with the SPDP disulfide **cross-linker** included **immunoconjugates** made with N-succinimidyl 4-[(iodoacetyl)amino]benzoate, the thioether **crosslinker**; with N-succinimidyl 3-(2-pyridyldithio)butyrate, hindered disulfide **cross-linker**; with a peptide spacer between the antibody and **cross-linker**; or with the dodecapeptide corresponding to the C-terminus of ricin A chain. The cytotoxic activities of the **immunoconjugates** and their susceptibility to reduction by glutathione in vitro were compared. The thioether-linked immunotoxin could not be cleaved by glutathione in vitro and had low cytotoxic potency, consistent with the requirement of a reducible disulfide linkage for activity. The hindered disulfide-linked immunotoxin was 3-fold more stable to reduction than the immunotoxin containing a standard unhindered disulfide linkage, but the cytotoxic activities of the two constructs were indistinguishable. The introduction of a flexible peptide Ala-Ala-Pro-Ala-Ala-Ala-Pro-Ala-Pro-Ala between Fib75 and the disulfide linkage introduced by N-succinimidyl 3-(2-pyridyldithio)propionate had no deleterious effect on cytotoxic activity and no effect on the

susceptibility of the disulfide linkage to reduction The enforced proximity of the A chain to the antibody caused by the use of a short chemical **cross-linker** in a conventional immunotoxin has no influence on either of these properties in this system. In contrast, substitution of the ricin A chain by a dodecapeptide, dinitrophenyl-Val-Tyr-Arg-Cys-Ala-Pro-Pro-Pro-Ser-Ser-Gln-Phe, greatly increased the extent to which the disulfide bond was cleaved by glutathione, demonstrating that the stability of the bond also depends upon the intact structure of the A chain.

ST ricin A chain immunotoxin structure activity; cytotoxic ricin immunotoxin prepn structure; antibody ricin A chain immunotoxin

IT Linking agents
(for ricin A-chain immunotoxins, structure-cytotoxicity relationship of)

IT Neoplasm inhibitors
(ricin A-chain immunotoxins as, preparation and cytotoxicity of, linking agent structure in relation to)

IT Molecular structure-biological activity relationship
(cytotoxic, of ricin A-chain immunotoxins, linkers in relation to)

IT Pharmaceutical dosage forms
(immunotoxins, ricin A-chain containing, preparation and cytotoxicity of, linking agents effect on, structure in relation to)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, **conjugates** with ricin A-chain, cytotoxicity of, linking agent structure in relation to)

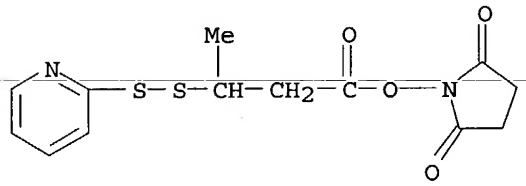
IT 68181-17-9 72252-96-1 **107348-47-0** 143294-44-4
RL: BIOL (Biological study)
(linkers for ricin A-chain immunotoxin, cytotoxicity and stability in relation to)

IT 143294-45-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and **conjugation** with monoclonal antibodies)

IT **107348-47-0**
RL: BIOL (Biological study)
(linkers for ricin A-chain immunotoxin, cytotoxicity and stability in relation to)

RN 107348-47-0 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:120495 HCAPLUS

DN 116:120495

ED Entered STN: 03 Apr 1992

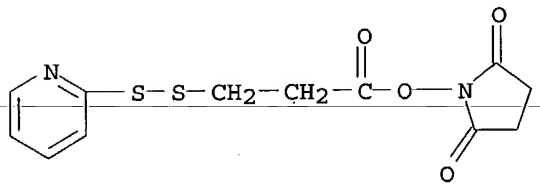
TI Immunoconjugates containing novel maytansinoids: promising anticancer drugs

AU Chari, Ravi V. J.; Martell, Bridget A.; Gross, Jonathan L.; Cook, Sherrilyn B.; Shah, Sudhir A.; Blattler, Walter A.; McKenzie, Sara J.; Goldmacher, Victor S.

CS **ImmunoGen, Inc., Cambridge, MA, 02139, USA**

SO Cancer Research (**1992**), 52(1), 127-31

CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
CC 1-6 (Pharmacology)
AB The potential of immunoconjugates of cytotoxic drugs for the treatment of cancer has not yet been realized owing to the difficulty of delivering therapeutic concns. of these drugs to the target cells. In an effort to overcome this problem the authors have synthesized maytansinoids that have 100- to 1000-fold higher cytotoxic potency than clin. used anticancer drugs. These maytansinoids are linked to antibodies via disulfide bonds, which ensures the release of fully active drug inside the cells. The conjugates show high antigen-specific cytotoxicity for cultured human cancer cells (50% inhibiting concentration, 10 to 40 pM), low systemic toxicity in mice, and good pharmacokinetic behavior.
ST maytansinoid immunoconjugate anticancer
IT Neoplasm inhibitors
(maytansinoid immunoconjugates as, in humans and laboratory animals)
IT Antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(monoclonal, conjugates, with maytansinoids, preparation and antitumor activity of, in humans and laboratory animals)
IT 64987-85-5 **68181-17-9**, N-Succinimidyl-3-(2-pyridyldithio)propionate
RL: BIOL (Biological study)
(immunoconjugates preparation with, as crosslinking reagent)
IT 139504-50-0DP, monoclonal antibody TA.1 conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of, in humans and laboratory animals)
IT 138148-68-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)
IT **68181-17-9**, N-Succinimidyl-3-(2-pyridyldithio)propionate
RL: BIOL (Biological study)
(immunoconjugates preparation with, as crosslinking reagent)
RN 68181-17-9 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:113497 HCAPLUS
DN 116:113497
ED Entered STN: 20 Mar 1992
TI **Immunoconjugates** for the treatment of Hodgkin's disease
IN Thorpe, Philip E.; Engert, Andreas
PA Imperial Cancer Research Technology Ltd., UK; Parker, David L.
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9107941	A2	19910613	WO 1990-US6801	19901120 <--
	WO 9107941	A3	19910711		
	W: AT, AU, BB, BG, BR, CA, CH, DE, DK, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU				
	RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
	US 5165923	A	19921124	US 1989-440050	19891120 <--
	AU 9169053	A1	19910626	AU 1991-69053	19901120 <--
	EP 502101	A1	19920909	EP 1991-900487	19901120 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
PRAI	US 1989-440050		19891120 <--		
	WO 1990-US6801		19901120 <--		

AB The compns. include a Hodgkin's disease cell-binding ligand **conjugated** to a toxin A chain moiety, such as ricin A chain or deglycosylated ricin A chain, dgA, by means of a **cross-linker** or other **conjugation** with a disulfide bond. In preferred aspects, therapeutic amts. of **conjugates** composed of a CD-30 or IRac antibody, or fragment thereof **conjugated** to deglycosylated A chain by means of an SMPT [N-succinimidyloxycarbonyl-α-methyl-α-(2-pyridyldithio)toluene] linker is administered to a Hodgkin's disease patient so as to selectively eliminate Hodgkin's disease cells. Also disclosed are particular hybridomas and monoclonal antibodies, and associated methodol., which may be employed, e.g., in the preparation of these immunotoxins, as well as other uses e.g. diagnostic applications. The mouse monoclonal antibodies HRS-3 and IRac (preparation given) were **conjugated** to dgA, using the SMPT linker. The administration of HRS-3.dgA and/or IRac.dgA (48 μg protein each), reduced the size of L540 tumor in mice and inhibited the relapse.

ST Hodgkins disease drug **immunoconjugate**

IT Ricins
RL: BIOL (Biological study)
(A chain or deglycosylated A chain, Hodgkin's disease treatment with)

IT Pseudomonas
(exotoxin of, **conjugates** with antibodies, Hodgkin's disease treatment with)

IT Neoplasm inhibitors
(**immunoconjugates**, for Hodgkin's disease treatment)

IT Toxins
RL: BIOL (Biological study)
(ribosome-inactivating, **conjugates** with antibodies, Hodgkin's disease treatment with)

IT Hodgkin's disease
(treatment of, with antibody-**conjugated** toxins)

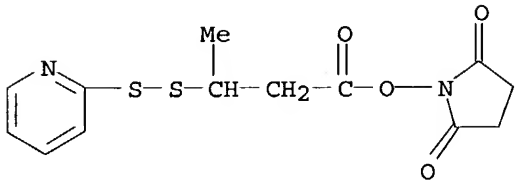
IT Toxins
RL: BIOL (Biological study)
(exo-, of Pseudomonas, **conjugates** with antibodies, Hodgkin's disease treatment with)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, **conjugates** with toxins, for Hodgkin's disease treatment)

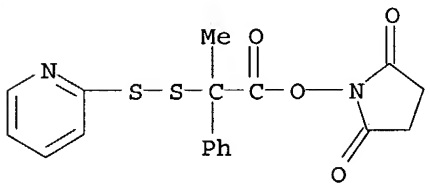
IT **107348-47-0 123266-19-3**
RL: BIOL (Biological study)
(linker, in preparation of immunotoxin **conjugates**, for Hodgkin's disease treatment)

IT **107348-47-0 123266-19-3**
RL: BIOL (Biological study)
(linker, in preparation of immunotoxin **conjugates**, for Hodgkin's

disease treatment)
RN 107348-47-0 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



RN 123266-19-3 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-phenyl-2-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:556658 HCAPLUS
DN 115:156658
ED Entered STN: 18 Oct 1991
TI Terminal-modified polylysine-based chelating polymers: highly efficient coupling to antibody with minimal loss in immunoreactivity
AU Slinkin, M. A.; Klibanov, A. L.; Torchilin, V. P.
CS Lab. Enzyme Eng., Moscow, 121552, USSR
SO Bioconjugate Chemistry (**1991**), 2(5), 342-8
CODEN: BCCHES; ISSN: 1043-1802
DT Journal
LA English
CC 15-3 (Immunochemistry)
AB A method is suggested for the preparation of chelating polymers containing a single terminal reactive group capable of interaction with proteins. These polymers were synthesized from N-CBZ-polylysine and DTPA and contain a terminal SH- or pyridyldisulfide group. A polymer mol. with MW 13,500 is able to carry up to 40 DTPA residues. Polymers easily and quant. bind with antibodies (Fab fragments of antimyosin antibodies R11D10) with minimal effect on antibody immunoreactivity as revealed in ELISA assay and in direct immunoanal. **Conjugates** prepared can chelate radioactive metal ions reaching very high specific radioactivity (>1 mCi 111In/10 μg of protein). Perspectives for their application are discussed.
ST polylysine chelating polymer antibody
IT Myosins
RL: PREP (Preparation)
(antibodies to, Fab fragment of, reaction products with modified polysine derivative, preparation of, as chelating polymer)
IT Chelating agents
(terminal-modified polysine **conjugates** with antibodies)
IT Antibodies
RL: PREP (Preparation)

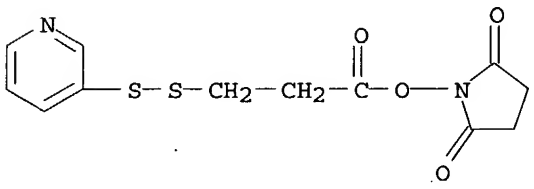
(to myosin, Fab fragment of, reaction products with modified polysine derivative, preparation of, as chelating polymer)

IT 3483-12-3DP, Dithiothreitol, reaction products with polylysine derivative and pyridyldithiopropionate derivative and DTPA and antibodies 23911-26-4DP, DTPA cyclic anhydride, reaction products with polylysine derivative and pyridyldithiopropionate derivative and antibodies 67178-46-5DP, reaction products with pyridyldithiopropionate derivative and DTPA and antibodies **126144-47-6DP**, reaction products with polylysine derivative and DTPA and antibodies
RL: PREP (Preparation)
(preparation of, as chelating polymer)

IT **126144-47-6DP**, reaction products with polylysine derivative and DTPA and antibodies
RL: PREP (Preparation)
(preparation of, as chelating polymer)

RN 126144-47-6 HCAPLUS

CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(3-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1990:164934 HCAPLUS

DN 112:164934

ED Entered STN: 28 Apr 1990

TI Synthesis and use of CD4 antigen peptide derivatives as antiretroviral agents

PA Genelabs, Inc., USA

SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2

DT Patent

LA English

IC C07C009-00; C07C009-22; A61K037-02

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8903813	A1	19890505	WO 1988-US3592	19881013 <--
	W: AU, DK, FI, HU, JP, KR, US				
	RW: AT, BE, BJ, CF, CG, CH, CM, DE, FR, GA, IT, LU, ML, MR, NL, SE, SN, TD, TG				
	AU 8927874	A1	19890523	AU 1989-27874	19881013 <--
	ZA 8807653	A	19891025	ZA 1988-7653	19881013 <--
	EP 394297	A1	19901031	EP 1988-909915	19881013 <--
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 03501847	T2	19910425	JP 1988-509140	19881013 <--
	ZA 8808173	A	19891129	ZA 1988-8173	19881101 <--
	DK 9000921	A	19900613	DK 1990-921	19900411 <--
PRAI	US 1987-108160		19871013 <--		
	US 1988-203285		19880601 <--		
	WO 1988-US3592		19881013 <--		

AB Polypeptides containing ≥7 consecutive amino acids of CD4 in which ≥1 of the heteroatoms of ≥1 amino acids (other than the

peptide bond atoms) are derivatized are prepared These polypeptide derivs. are capable of modulating CD4-dependent retrovirus-induced cellular responses. Many polypeptides having a core sequence of Thr-Tyr-Ile-Cys-Glu-Val-Glu and various degrees of side-chain benzylation were prepared by solid phase peptide synthesis. Many were more effective than the underivatized polypeptides at inhibiting cell fusion induced by human immunodeficiency viruses (HIVs) as well as at reducing infectivity of these viruses. The derivs. were effective against multiple distinct isolates of HIV-1 and HIV-2.

ST CD4 antigen polypeptide deriv retrovirus infection; human immunodeficiency virus CD4 peptide deriv; HIV infection CD4 peptide deriv

IT Fusion, biological
(retrovirus-induced, inhibition of, CD4 antigen peptide derivs. for)

IT Antigens
RL: BIOL (Biological study)
(CD4, polypeptides of, derivs. of, for use as antiretroviral agents)

IT Virus, animal
(human immunodeficiency 1, protection from, CD4 antigen peptide derivs. for)

IT Virus, animal
(human immunodeficiency 2, protection from, CD4 antigen peptide derivs. for)

IT Virus, animal
(retro-, CD4 antigen-dependent, protection from, CD4 antigen peptide derivs. for)

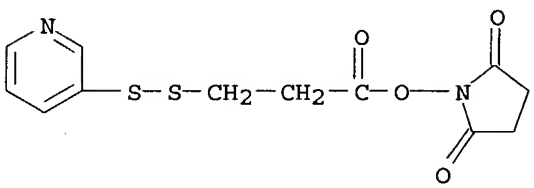
IT 126144-44-3D, Aralkyl side-chain derivs.
RL: BIOL (Biological study)
(polypeptides containing, as antiretroviral agents)

IT 100-39-0DP, α-Bromotoluene, reaction products with CD4 peptides 611-17-6DP, 2-Chlorobenzyl bromide, reaction products with CD4 peptides 28777-60-8DP, reaction products with CD4 peptides 35884-77-6DP, Xylyl bromide, reaction products with CD4 peptides 64987-85-5DP, reaction products with CD4 peptides 123380-67-6DP, aralkyl derivs. 123380-68-7P 124699-87-2P 124699-88-3P 124699-90-7P 124699-91-8P 124699-92-9P 124699-93-0P 124699-95-2P 124722-72-1P 124722-73-2P 124722-74-3P 126144-46-5DP, benzyl derivs. **126144-47-6DP**, reaction products with CD4 peptides 126144-48-7P 126144-49-8P 126144-50-1P 126144-51-2P 126144-52-3P 126144-53-4P 126144-54-5P 126144-56-7P 126144-57-8P 126144-58-9P 126144-59-0P 126164-12-3P
RL: PREP (Preparation)
(preparation of, for inhibition of human immunodeficiency virus-induced cell fusion and infectivity)

IT **126144-47-6DP**, reaction products with CD4 peptides
RL: PREP (Preparation)
(preparation of, for inhibition of human immunodeficiency virus-induced cell fusion and infectivity)

RN 126144-47-6 HCAPLUS

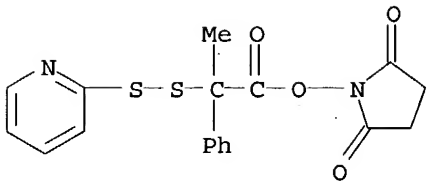
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(3-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1990:96500 HCAPLUS

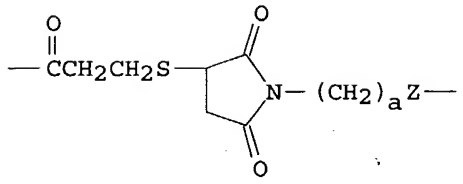
DN 112:96500
ED Entered STN: 18 Mar 1990
TI Preparation and characterization of **conjugates** of recombinant CD4 and deglycosylated ricin A chain using different **cross-linkers**
AU Ghetie, Victor; Till, Mark A.; Ghetie, Maria Ana; Tucker, Thomas; Porter, Jim; Patzer, Eric J.; Richardson, James A.; Uhr, Jonathan W.; Vitetta, Ellen S.
CS Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235, USA
SO Bioconjugate Chemistry (**1990**), 1(1), 24-31
CODEN: BCCHES; ISSN: 1043-1802
DT Journal
LA English
CC 15-2 (Immunochemistry)
Section cross-reference(s): 1, 63
AB In a previous study, it was demonstrated that **conjugates** containing soluble, recombinant human CD4 (rCD4) and the deglycosylated form of ricin A chain (dgA) (rCD4-dgA) effectively kill a human T cell line infected with the human immunodeficiency virus (HIV) in vitro. In contrast, such **conjugates** are 100-1000-fold less toxic to uninfected cells. In order to use a rCD4-dgA **conjugate** effectively in vivo, it was important to demonstrate that (1) it binds to and kills HIV-infected, but not uninfected, human cells, (2) it is stable in the circulation, and (3) it has an optimal therapeutic index (toxicity to animals vs. toxicity to target cells). A major factor affecting the efficacy of such **conjugates** in vitro and in vivo is the nature of the **cross-linker** between the ligand (rCD4) and the toxin (dgA). In this report, rCD4-dgA **conjugates** were prepared using three different **cross-linkers.** Different methods of purification have been compared by determining the optimal yield, purity, and retention of biol. activity (i.e., binding to gp120 and dgA chain activity). The structure of these **conjugates** as well as their cytotoxicity to target cells in vitro was analyzed. Their pharmacokinetics, tissue localization, and toxicity were compared in mice.
ST CD4 antigen ricin A chain **conjugate**
IT Ricins
RL: PREP (Preparation)
(A chain of, deglycosylated, **conjugates** with CD4 antigen, preparation and biol. and structural characterization of)
IT Antigens
RL: PREP (Preparation)
(CD4, **conjugates** with deglycosylated ricin A chain, preparation using different **crosslinkers** and biol. and structural characterization of)
IT Immunodeficiency
(acquired immune deficiency syndrome, treatment of, CD4 antigen **conjugate** with ricin A chain for)
IT Virus, animal
(human immunodeficiency, infection with, of cells, treatment of, CD4 antigen **conjugates** with ricin A chain for)
IT 64987-85-5 76931-93-6 **123266-19-3**
RL: BIOL (Biological study)
(CD4 antigen **crosslinking** to ricin A mediated by)
IT **123266-19-3**
RL: BIOL (Biological study)
(CD4 antigen **crosslinking** to ricin A mediated by)
RN 123266-19-3 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-phenyl-2-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



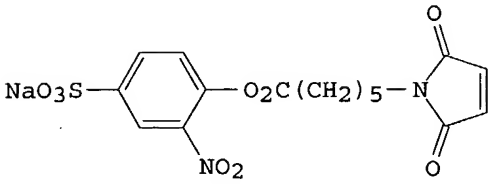
L38 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:428516 HCAPLUS
DN 111:28516
ED Entered STN: 21 Jul 1989
TI Solubilization of proteins for pharmaceutical compositions using polyproline **conjugation**
IN Aldwin, Lois; Nitecki, Danute E.
PA Cetus Corp., USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-00
ICS C07K003-08; C07K017-00
ICA C07K013-00; A61K037-02; C12P021-02
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8803412	A1	19880519	WO 1987-US2930	19871110 <--
	W: AU, DK, FI, JP, NO				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4894226	A	19900116	US 1986-931197	19861114 <--
	AU 8783264	A1	19880601	AU 1987-83264	19871110 <--
	AU 626518	B2	19920806		
	EP 305409	A1	19890308	EP 1987-907713	19871110 <--
	EP 305409	B1	19911030		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 68976	E	19911115	AT 1987-907713	19871110 <--
	CA 1305051	A1	19920714	CA 1987-551549	19871110 <--
PRAI	US 1986-931197		19861114 <--		
	EP 1987-907713		19871110 <--		
	WO 1987-US2930		19871110 <--		

GI



I



II

AB Soluble aqueous pharmaceutical compns. comprise a biol. active protein covalently **conjugated** to polyproline via the flexible spacer arm I [a ≥1; Z = CO, CONH(CH2)xO[(CH2)y]nO(CH2)zNHCO(CH2)bCO; x, y, z = 2-4, b = 2, 3; n = 1-10], which is derived in part from the 6-maleimidocaproate II. The **unconjugated** protein is not readily soluble in the aqueous carrier at pH 6-8 in the absence of a solubilizing agent. Polyproline was treated with 4-hydroxy-3-nitrobenzenesulfonic acid 3-(2-pyridyldithio)propionate (preparation given), followed by reaction with dithiothreitol to give polypro-NCOCH2CH2SH. The modified polyproline was treated with II, which was prepared by treating 6-maleimidocaproic acid with Na 4-hydroxy-3-nitrobenzenesulfonate. This modified polymer was lyophilized and treated with a recombinant human des-alanyl1-ser125IL-2 to give a modified polyproline-IL-2 **conjugate** (III). In rats, the half-life plasma levels of III and **unconjugated** IL-2 were the same at 8000 and 800 U/mL (4, 6 min and 26, 28 min, resp.), but in the third phase (t 1/2 for 80 U/mL) the half-life for III was 3.3 h whereas the half-life for IL-2 was 1.4 h.

ST polyproline protein **conjugate** solubilization; interleukin 2 polyproline **conjugate** solubilization

IT Interferons
RL: BIOL (Biological study)
(**conjugates** with polyproline, for improved solubility)

IT Solubilization
(of proteins, by **conjugation** with polyproline)

IT Proteins, specific or class
RL: BIOL (Biological study)
(**conjugates**, with polyproline, for improved solubility)

IT Toxins
RL: BIOL (Biological study)
(immuno-, **conjugates** of with polyproline, for improved solubility)

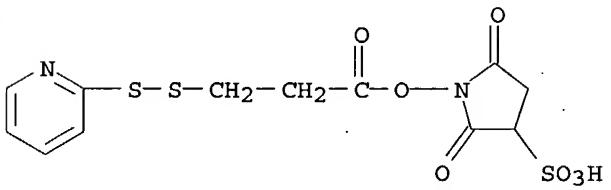
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 2, **conjugates** with polyproline, for improved solubility)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukins, **conjugates** with polyproline, for improved solubility)

IT 55750-53-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with hydroxynitrobenzenesulfonate)

IT 68181-17-9P 121115-29-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

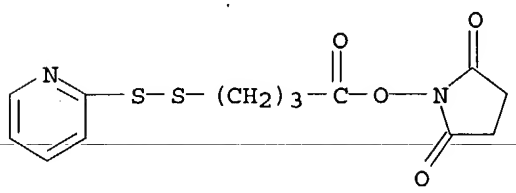
(Reactant or reagent)
(preparation and reaction of, with polyproline)
IT 101554-76-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with N-(mercaptopropionyl)polyproline)
IT 25191-13-3DP, Polyproline, **conjugates** with insol. proteins
25213-33-6DP, Polyproline, **conjugates** with insol. proteins
62683-29-8DP, Colony-stimulating factor, polyproline **conjugates**
90598-63-3DP, polyproline **conjugates** 94218-72-1DP, Interleukin 2 (human clone pTIL2-21a protein moiety), polyproline **conjugates**
110942-02-4DP, polyproline **conjugates** 121338-29-2DP, 9-157-Tumor necrosis factor (human), polyproline **conjugates**
RL: PREP (Preparation)
(preparation of, for improved solubility)
IT 6313-34-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (pyridyldithio)propionic acid)
IT 68617-64-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydroxynitrobenzenesulfonate)
IT **121115-30-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with polyproline)
IT **121115-30-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with polyproline)
RN 121115-30-8 HCAPLUS
CN 3-Pyrrolidinesulfonic acid, 2,5-dioxo-1-[1-oxo-3-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:417026 HCAPLUS
DN 109:17026
ED Entered STN: 22 Jul 1988
TI Manufacture of antitumor tumor necrosis factor-immunoglobulin **complex**
IN Tsubochi, Jiro; Kazama, Mutsumi; Ishii, Hidemi; Mizuno, Denichi
PA Research Development Corp. of Japan, Japan
SO Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07K015-12
ICS C07K003-08
ICA A61K039-395
CC 1-6 (Pharmacology)
Section cross-reference(s): 15, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62190200	A2	19870820	JP 1986-30624	19860217 <--

PRAI JP 1986-30624 19860217 <--
AB Igs or their fragments are covalently bound to rabbit tumor necrosis factor (TNF) to form an antitumor protein **complex.** N-[3-(2-Pyridyl)dithiopropionyl]-TNF and reduced IgM (antifibrin antibody) were reacted to form a **complex** (mol. weight .apprx.2 + 106).
ST antitumor Ig tumor necrosis factor **complex**
IT Fibrins
RL: BIOL (Biological study)
(antibody to, of human, **complex** with tumor necrosis factor)
IT Immunoglobulins
RL: BIOL (Biological study)
(**complexes** with tumor necrosis factor, as neoplasm inhibitor, tissue targeting in relation to)
IT Neoplasm inhibitors
(tumor necrosis factor-IgM **complexes**)
IT Immunoglobulins
RL: BIOL (Biological study)
(M, **complexes** with tumor necrosis factor, as neoplasm inhibitor, tissue targeting in relation to)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(tumor necrosis factor, **complexes** with Igs, as neoplasm inhibitor, tissue targeting in relation to)
IT **115088-06-7DP, complexes** with tumor necrosis factor and IgM
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as neoplasm inhibitor, tissue targeting in relation to)
IT **115088-06-7DP, complexes** with tumor necrosis factor and IgM
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as neoplasm inhibitor, tissue targeting in relation to)
RN 115088-06-7 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-4-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:131318 HCAPLUS
DN 106:131318
ED Entered STN: 01 May 1987
TI Effect of linkage variation on pharmacokinetics of ricin A chain-antibody **conjugates** in normal rats
AU Worrell, N. R.; Cumber, A. J.; Parnell, G. D.; Mirza, A.; Forrester, J. A.; Ross, W. C. J.
CS Div. Biol., Inst. Cancer Res., London, SW3, UK
SO Anti-Cancer Drug Design (**1986**), 1(3), 179-88
CODEN: ACDDEA; ISSN: 0266-9536
DT Journal
LA English

CC 1-6 (Pharmacology)
Section cross-reference(s): 15, 25, 27

AB The pharmacokinetics of 3 ricin A chain-antibody **conjugates** having different bridging structures were studied. The 1st **conjugate** has a disulfide linkage and was prepared with the N-succinimidyl 3-(2-pyridyldithio)propionate **crosslinking** reagent. The 2nd **conjugate** has a protected disulfide linkage with a Me group substituted on the C atom of the bridging structure adjacent to the disulfide linkage. Its preparation necessitated the preparation of a new **crosslinking** reagent N-succinimidyl 3-(2-pyridyldithio)butyrate. The 3rd **conjugate** has a sulfide linkage and was prepared with the **crosslinking** reagent N-succinimidyl 4-(iodoacetylamino)benzoate which was preparation by a novel route. The 1st **conjugate** is reducible, the 2nd less easily reducible and the 3rd cannot be reduced. On administration to animals all 3 **conjugates** displayed biphasic kinetics. The reducibility of the bond had no significant effect on the early disappearance of the **conjugate** from the circulation. However, at the later time points ease of reduction of the bond was associated with a more rapid disappearance of **conjugate**.

ST ricin A antibody **conjugate**; **crosslinking** ricin A antibody

IT Neoplasm inhibitors
(antibody **conjugates** with ricin A chain, succinimidyl ester-**crosslinked**, preparation and pharmacokinetics of)

IT Kinetics of reduction
(of (pyridyldithio)alkanoic acids)

IT **Crosslinking** agents
(succinimidyl esters, in preparation of ricin A chain-antibody **conjugates**)

IT Ricins
RL: SPN (Synthetic preparation); PREP (Preparation)
(A, chain, **conjugates** with antibodies, preparation and pharmacokinetics of)

IT Antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(monoclonal, reaction products, with succinimidyl esters, ricin A chain **conjugates**, preparation and pharmacokinetics of)

IT 79-04-9, Chloroacetyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(chloroacetylation by, of aminobenzoic acid)

IT 150-13-0, 4-Aminobenzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(chloroacetylation of)

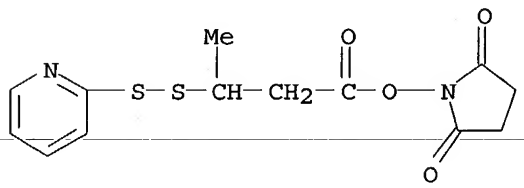
IT 4596-39-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion to iodo derivs.)

IT 63684-46-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

IT 68181-17-9DP, N-Succinimidyl 3-(2-pyridyldithio)propionate, reaction products with antibodies, **conjugates** with ricin A chain 72252-96-1DP, reaction products with antibodies, **conjugates** with ricin A chain **107348-47-0DP**, reaction products with antibodies, **conjugates** with ricin A chain
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and pharmacokinetics of)

IT 5434-66-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with hydroxysuccinimide)

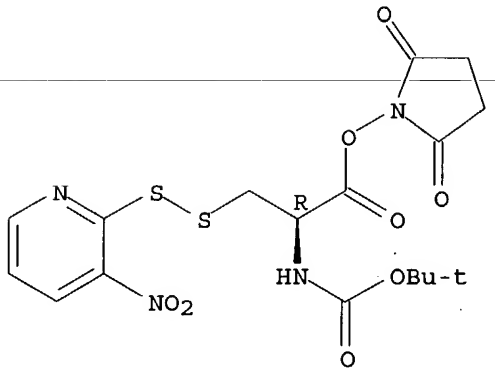
IT 107348-48-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with hydroxysuccinimide and reduction kinetics of)
IT 59089-57-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with mercaptoalkanoic acids)
IT 26473-49-4P, 3-Mercaptobutyric acid 59729-24-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with pyridinesulfenyl chloride)
IT 68617-64-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and reduction kinetics of)
IT 6066-82-6, N-Hydroxysuccinimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with (pyridyldithio)butyric acid or iodoacetylaminobenzoic acid)
IT 507-09-5, Thioacetic acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with alkylacrylic acids)
IT 2127-03-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with chlorine)
IT 541-47-9, 3,3-Dimethylacrylic acid 3724-65-0, Crotonic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with thioacetic acid)
IT 107348-49-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of, kinetics of)
IT **107348-47-0DP**, reaction products with antibodies, **conjugates** with ricin A chain
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and pharmacokinetics of)
RN 107348-47-0 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(2-pyridinyldithio)butoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1986:65315 HCAPLUS
DN 104:65315
ED Entered STN: 08 Mar 1986
TI The N-hydroxysuccinimide ester of Boc-[S-(3-nitro-2-pyridinesulfenyl)]-cysteine: a heterobifunctional **cross-linking** agent
AU Bernatowicz, Michael S.; Matsueda, Gary R.
CS Cell. Mol. Res. Lab., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
SO Biochemical and Biophysical Research Communications (**1985**), 132(3), 1046-50
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English

CC 9-10 (Biochemical Methods)
AB Synthetic cysteine-containing peptides were unidirectionally **conjugated** to albumin via disulfide bonds by using the S-(3-nitro-2-pyridinesulfenyl) derivative of cysteine. This method employs the N-hydroxysuccinimide ester of Boc-[S-(3-nitro-2-pyridinesulfenyl)]-cysteine, a protected amino acid derivative used in peptide synthesis, as a heterobifunctional **crosslinking** agent. The disulfide bonds in the **conjugates** are formed by the reaction of free thiols with S-(3-nitro-2-pyridinesulfenyl) groups. Bovine albumin was **conjugated** in this manner to several **conjugates** demonstrated incorporations of from 6 to 11 peptide mols./mol. protein.
ST albumin synthetic peptide **conjugation crosslinking**; nitropyridinesulfenylcysteine hydroxysuccinimide ester albumin peptide
IT Peptides, compounds
RL: PREP (Preparation)
(reaction products with albumin, heterobifunctional **crosslinking** agent forprepn. of)
IT Albumins
RL: PREP (Preparation)
(reaction products with synthetic peptides, heterobifunctional **crosslinking** agents for preparation of)
IT **100108-75-6P**
RL: PREP (Preparation)
(preparation of, as heterobifunctional **crosslinking** agent, in albumin **conjugation** to synthetic peptides)
IT 88497-76-1DP, reaction products with albumin 100108-76-7P
RL: PREP (Preparation)
(preparation of, heterobifunctional **crosslinking** agent for)
IT 100155-62-2DP, reaction products with albumin
RL: PREP (Preparation)
(preparation of, heterobifunctional **crosslinking** agents for)
IT **100108-75-6P**
RL: PREP (Preparation)
(preparation of, as heterobifunctional **crosslinking** agent, in albumin **conjugation** to synthetic peptides)
RN 100108-75-6 HCAPLUS
CN Carbamic acid, [2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1-[[(3-nitro-2-pyridinyl)dithio]methyl]-2-oxoethyl]-, 1,1-dimethylethyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

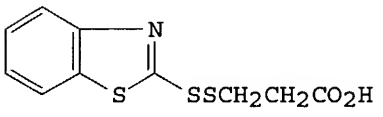


L38 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:426430 HCAPLUS
DN 93:26430
ED Entered STN: 12 May 1984

TI Disulfide derivatives
IN Fujii, Tadashiro; Nakagawa, Nobuaki; Kotani, Kikuo
PA Toyo Jozo Co., Ltd., Japan
SO Ger. Offen., 31 pp.
CODEN: GWXXBX
DT Patent
LA German
IC C07D277-78; C07D213-89
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 27, 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2928384	A1	19800207	DE 1979-2928384	19790713 <--
	DE 2928384	C2	19890105		
	JP 55017302	A2	19800206	JP 1978-85900	19780713 <--
	JP 60058232	B4	19851219		
	FR 2430943	A1	19800208	FR 1979-18007	19790711 <--
	FR 2430943	B1	19830114		
	GB 2029825	A	19800326	GB 1979-24336	19790712 <--
	GB 2029825	B2	19830119		
	US 4258193	A	19810324	US 1979-57502	19790713 <--
PRAI	JP 1978-85900		19780713 <--		

GI



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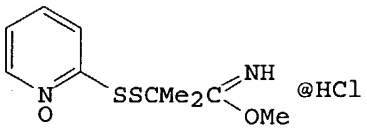


II

AB A series of .apprx.30 (heterocyclyldithio)alkanoic acids and derivs. was prepared as exchange and **crosslinking** agents for proteins, e.g., insulin. Thus, 2,2'-dithiobis(benzothiazole) and HSCH2CH2CO2H in C6H6 were heated 3 h at 70° with stirring to give I, which was converted into the acid chloride or esterified with, e.g., hydroxysuccinimide. Also prepd, was, e.g., II.

ST protein **crosslinking** dithioalkanoic acid; benzothiazolyldithioalkanoic acid; pyridyldithioalkanoic acid

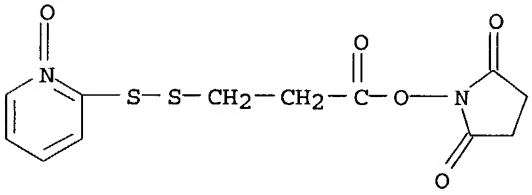
IT Proteins
RL: RCT (Reactant); RACT (Reactant or reagent)
(**crosslinking** of, with (heterocyclyldithio)alkanoic acids and derivs.)

IT 9004-10-8, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(**crosslinking** of, with (heterocyclyldithio)alkanoic acids and derivs.)

IT 59006-14-3P 72632-26-9P 72632-27-0P 72632-29-2P 72632-30-5P
72632-31-6P 72632-32-7P 72632-33-8P 72632-37-2P 72632-38-3P
72632-39-4P 72632-40-7P 72632-41-8P 72632-44-1P 72632-45-2P
72632-46-3P 72632-47-4P 72632-48-5P 72632-49-6P 72632-50-9P
72645-91-1P 72645-92-2P **73919-78-5P** 73919-79-6P
73919-80-9P 73919-81-0P 73919-82-1P 73952-12-2P 73952-13-3P
73952-14-4P 73952-15-5P
RL: PREP (Preparation)
(manufacture of, for use as exchange and **cross-linking** reagents for protein materials)

IT 72632-28-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and esterification with hydroxysuccinimide)

IT 72632-52-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and partial hydrolysis of)
IT 72632-24-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and transamination with ε-aminocaproic acid)
IT 72632-25-8P 72632-53-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, esterification, and conversion into acid chloride)
IT 107-96-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dithiobis[heterocycle])
IT 120-78-5 3696-28-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with mercaptoalkanoic acids)
IT **73919-78-5P**
RL: PREP (Preparation)
(manufacture of, for use as exchange and **cross-linking** reagents for protein materials)
RN 73919-78-5 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[3-[(1-oxido-2-pyridinyl)dithio]-1-oxopropoxy]- (9CI) (CA INDEX NAME)



L38 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1979:22821 HCAPLUS
DN 90:22821
ED Entered STN: 12 May 1984
TI Pyridine derivatives
IN Carlsson, Jan Per Erik; Axen, Rolf Erik Axel Verner; Drevin, Haakan Nils Yngve; Lindgren, Goran Einar Samuel
PA Pharmacia Fine Chemicals AB, Swed.
SO Ger. Offen., 22 pp.
CODEN: GWXXBX
DT Patent
LA German
IC C07D401-12
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2808523	A1	19780907	DE 1978-2808523	19780228 <--
	DE 2808523	C2	19871119		
	SE 7702462	A	19780905	SE 1977-2462	19770304 <--
	SE 430062	B	19831017		
	SE 430062	C	19840126		
	US 4149003	A	19790410	US 1978-882546	19780302 <--
	FR 2382450	A1	19780929	FR 1978-6161	19780303 <--
	FR 2382450	B1	19821105		
	GB 1597756	A	19810909	GB 1978-8456	19780303 <--

	JP 53130674	A2	19781114	JP 1978-24066	19780304 <--
	JP 61021227	B4	19860526		
	US 4563304	A	19860107	US 1984-582911	19840223 <--
	JP 61191675	A2	19860826	JP 1985-290918	19851225 <--
	JP 62004368	B4	19870130		
PRAI	SE 1977-2462		19770304 <--		
	US 1978-882546		19780302 <--		
	US 1978-946140		19780927 <--		
	US 1979-98302		19791128 <--		
	US 1981-238853		19810227 <--		
OS	CASREACT 90:22821				

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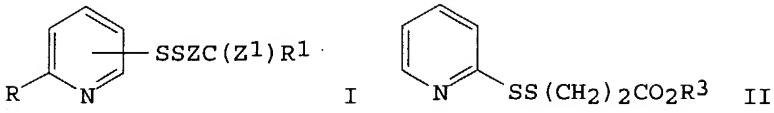


AB The pyridyl disulfides I [R = H, NO2; Z = C1-10 alkylene; Z1 = O, NH; R1 = pyridylthio, OR2 (R2 = Me, Et, succinimido, glutarimido)] were prepared for use as thiolating or coupling agents for polypeptides, proteins, etc. Thus, 2-pyridyl disulfide reacted with HS(CH2)2CO2H in AcOEt, followed by the addition of BF3.Et2O to give II (R3 = H), which was treated with N-hydroxysuccinimide and dicyclohexylcarbodiimide to give II (R3 = succinimido).

ST coupling agent pyridyl disulfide; thiolation pyridyl disulfide; pyridyl disulfide

IT Peptides, reactions
Proteins
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, by pyridyl disulfides)

IT Albumins, blood serum
RL: RCT (Reactant); RACT (Reactant or reagent)
(pyridyl disulfides as coupling and thiolating agent for)

IT Coupling agents
(pyridyl disulfides, for peptides and proteins)

IT Albumins, blood serum
RL: RCT (Reactant); RACT (Reactant or reagent)
(thiolation of)

IT Antibodies
(IgG, coupling of, to α-amylase, by pyridyl disulfide derivative)

IT Antibodies
(IgG, mercaptopropionyl derivative)

IT 9000-90-2DP, **conjugatee** with Schaf IgG antibody 9000-90-2DP, mercaptopropionyl derivative 9001-78-9P 68617-65-2P 68617-66-3P **68617-67-4P 68617-68-5P 68617-69-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

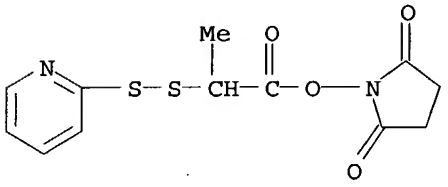
IT 68617-64-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, and reaction with hydroxysuccinimide)

IT 68181-17-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, and use as thiolating or coupling agent)

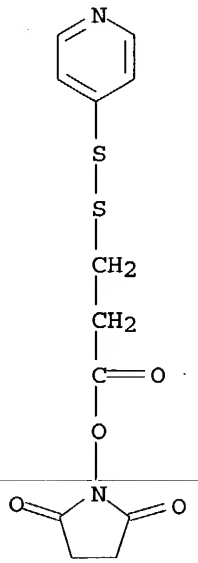
IT 6066-82-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carboxyethyl pyridyl disulfide)

IT 2127-03-9 2127-10-8 2645-22-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with mercaptopropionic acid)

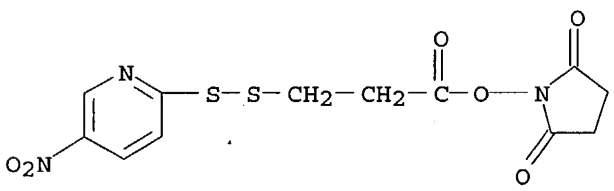
IT 79-42-5 107-96-0 50280-42-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with pyridyl disulfide)
IT 9000-90-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(thiolation of)
IT **68617-67-4P 68617-68-5P 68617-69-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 68617-67-4 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-2-(2-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



RN 68617-68-5 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[1-oxo-3-(4-pyridinyldithio)propoxy]- (9CI) (CA INDEX NAME)



RN 68617-69-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[3-[(5-nitro-2-pyridinyl)dithio]-1-oxopropoxy]- (9CI) (CA INDEX NAME)



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